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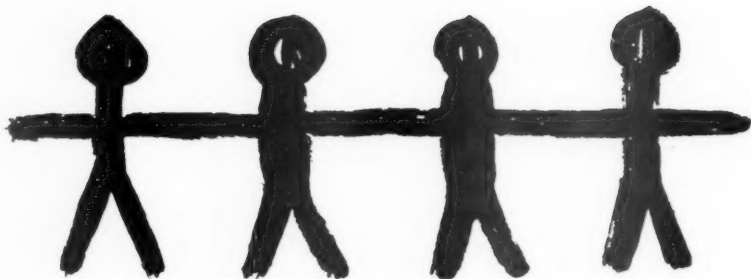
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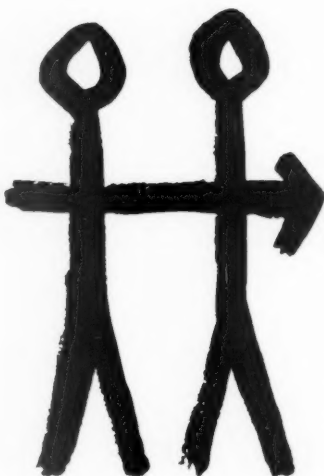
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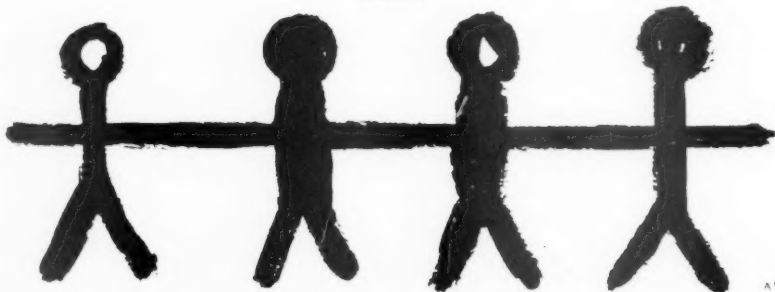
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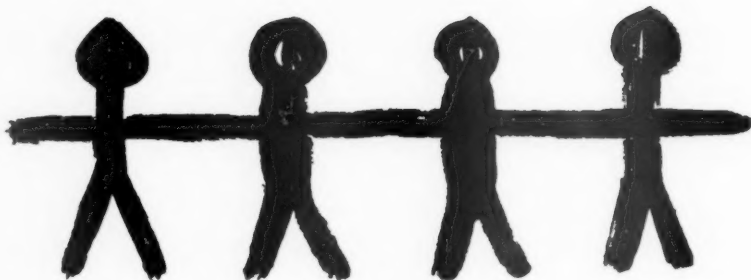
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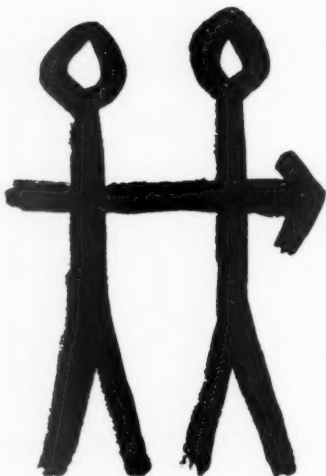
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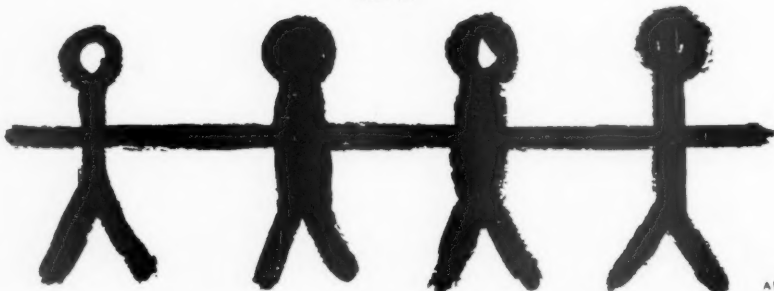
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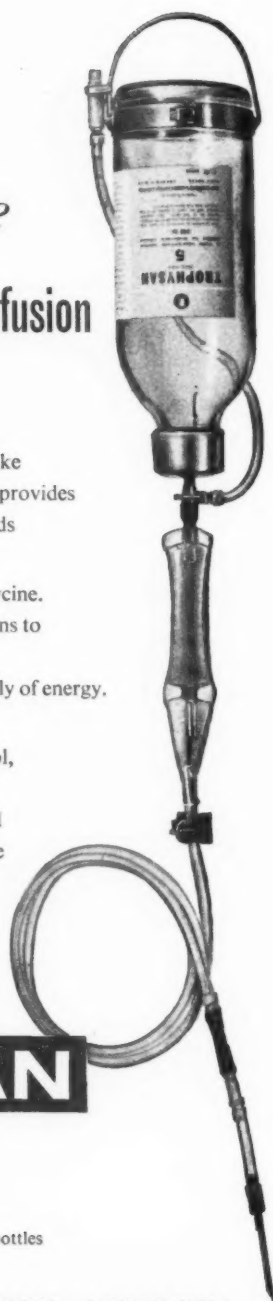
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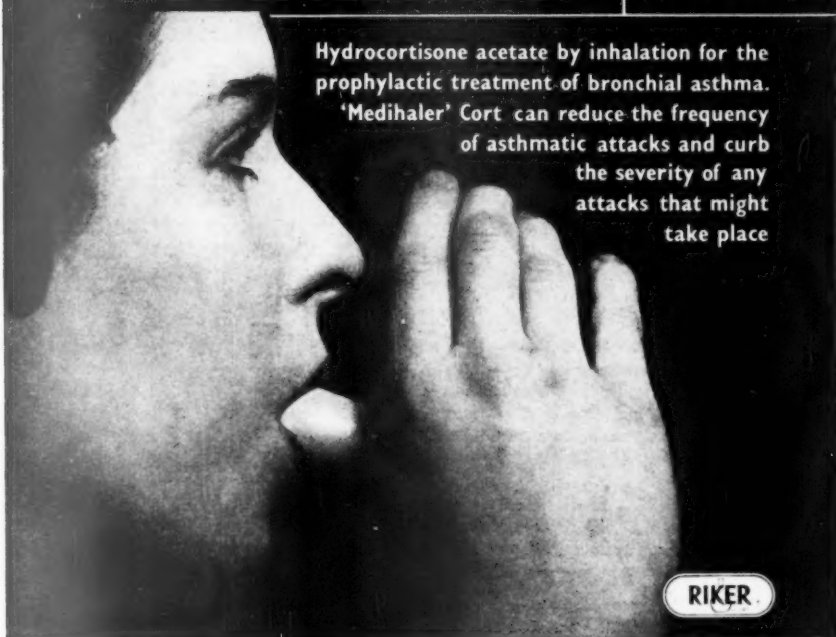
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Section of Psychiatry

President—ELIOT SLATER, M.D.

Meeting
January 13, 1959

DISCUSSION: INVESTIGATION OF OUTCOME OF TREATMENT OF DEPRESSION [Abridged]

Dr. J. M. White (Wakefield and Leeds):

*Factors Related to Outcome of Treatment
with E.C.T.*

Many problems on the treatment of depression with E.C.T. still exist, foremost among them being the prediction of the outcome of treatment. There is an extensive literature on prognostic factors, but these studies tend to be qualitative and impressionistic. There is a need for further investigation using all modern techniques of evaluation. In the papers by Dr. Hamilton and myself are presented a series of cases of depression who have been carefully studied clinically and closely followed-up after treatment with E.C.T., and in whom the clinical study and follow-up have been quantified by the use of a rating scale. The factors related to the outcome of treatment have been studied and an attempt made, in a group considered suitable for E.C.T. on general clinical grounds, to refine the indications for this treatment and to prognosticate more accurately its results.

The group studied comprised male in-patients who had been admitted to hospital with a depressive illness and who were considered likely to benefit from treatment with E.C.T. They had either attempted suicide before admission, or were considered serious suicidal risks, or could not be dealt with as out-patients because of the intensity of their symptoms or for social reasons, or in a small number of cases because of suspected or confirmed physical illness which required preliminary hospital care.

The outcome of treatment was then correlated with certain factors in the general clinical data. These included the family history, neurotic traits in childhood, neurotic traits in adult life, the mode of onset (sudden or gradual), the course of the illness (progressive or fluctuating), the duration of illness, physical and psychological precipitant factors, the number of previous attacks, diurnal variation, age, weight, Rees-Eysenck body index, blood pressure, Funkenstein test and Hobson score.

Of the 64 patients in this series, 13 did not receive E.C.T. for various reasons. Of these 13, 2 committed suicide, and only 5 recovered fully.

51 patients received E.C.T., the average course comprising 6 treatments. 43 recovered and were discharged from hospital, and one com-

mitted suicide. Contrasting the fully recovered with the rest, a statistical comparison of the treated and untreated groups showed the more favourable outcome in the former as highly significant ($\chi^2=11.6$, d.f.=1, $P<0.001$). However, of the 43 patients who responded satisfactorily to E.C.T., 15 relapsed. They recovered after a further course of E.C.T. and remained well. The patients who did not do well with E.C.T., with one exception, tended to form a homogeneous group. All but one were in the higher age-group. All were cases of severe endogenous depression. One could not say that this clinical picture was necessarily related to the poor outcome with E.C.T. as many other patients with endogenous depression showed good results. However, the principal failures were found in this group.

16 variables were correlated with outcome, and in only 4 was a significant relationship confirmed. The highest correlation was that of duration of illness (0.46), followed by weight (-0.31) and the body index (0.29). The findings for the Funkenstein test also showed a significant correlation with outcome. Age and blood pressure, usually accepted as influencing the outcome with E.C.T., showed in fact very low correlations. The Hobson score gave a low correlation with outcome (0.18). This score consists of 16 items which assess certain factors related to personality, intelligence and the development and symptoms of the illness. In Hobson's original paper (1953) a low score was highly correlated with a good response to treatment. Our findings did not confirm those originally reported. This may have been due to the difficulty we found in applying this tool, full and accurate information on which is difficult to elicit.

Many features of interest have emerged from this study. The clinical findings emphasize the value of E.C.T. Those with a history of short duration and pyknic body build and heavy body weight appear to do best with this treatment. Since even severe cases of endogenous depression may remit spontaneously over a period of some months, it is certainly worth waiting to see if spontaneous remission will develop when the administration of E.C.T. would involve a considerable danger to the life of the patient.

(Illustrative cases quoted.) The fact that our failures were mainly in the severe endogenous depression group is of interest and indicates that such features are not necessarily indicative of good prognosis as is generally assumed. The suicide in the treated group was unexpected and preceded by previous suicidal attempts of histrionic quality. 2 patients who had morbid fear of E.C.T., and who had previously refused to accept this treatment, committed suicide after ultimate acceptance of the treatment and before it could begin. I have little doubt that in these cases fear of E.C.T. acted as a powerful precipitant towards suicide.

Many difficulties arose in the course of this investigation. Our follow-up system worked imperfectly and did not take into account the fluctuations of the illness and the high incidence of relapses. To eliminate this problem the patients have been seen at more frequent intervals over a longer period. It is possible that the high incidence of relapse is related to the number of treatments initially given. It seems probable that a longer course of treatment would have been preferable in most cases and might have prevented a number of early relapses.

REFERENCE

HOBSON, R. F. (1953) *J. Neurol. Psychiat.*, **16**, 275.

Dr. Max Hamilton (Leeds):

Autonomic Function and Syndromes in Depression

Dr. White's paper gave an account of the relation between various factors in the patient's history and the outcome of treatment in depression. The present paper is concerned with the details of two of these factors.

Investigation of autonomic functions in relation to psychiatry has a long history, but in recent years interest has been concentrated chiefly on the Funkenstein test. As originally described, the test consists of graphing the changes in blood pressure which occur, first, after the intravenous injection of 0.025 mg. of adrenaline, and then, when the blood pressure has returned to its basal level, after the intramuscular injection of 10 mg. of Mecholyl, recorded for no longer than twenty-five minutes. Funkenstein and his colleagues (1952) classified the curves so obtained into 7 groups, and on the basis of their findings announced that Groups VI and VII had a good prognosis to treatment by E.C.T., regardless of the diagnosis of the patient. In recent years, it has been customary to omit the adrenaline, since it is not very informative. This has the effect of amalgamating Groups II and III, and V and VI.

Considering only the curves obtained after the injection of Mecholyl, Gellhorn (1953) classified the curves into those showing hyper-, normo-, and hypo-reactivity. He stated that the hypo-

reactive curves indicated a good prognosis after treatment.

Two difficulties arise: In the first place, a fair proportion of curves do not fit the classifications, and in the second (as shown by Munro, 1958), this method of classification has a good deal of unreliability, so that errors of classification form a large proportion of the total.

A new approach to the problem was attempted by the method of curve-fitting. The most appropriate curves to use would probably be either an exponential curve, comparable to the changes of temperature of a cold body in a warm room, or some form of cybernetic function. Unfortunately, for various reasons these are impracticable. In the end, it was decided that the simplest curve of all, i.e. a straight line, might give satisfactory results. The use of the best-fitting straight line converts the information in the Funkenstein curve into three parameters: Basal blood pressure, the drop of blood pressure, and the slope of the line. The first two are highly reliable measures with reliability coefficients of 0.80 and 0.75 respectively. The slope is unreliable, having a coefficient of 0.36. Since both the Funkenstein and Gellhorn classifications depend much on the slope of the curve, this accounts for the unreliability of classification.

The correlation between outcome after treatment and basal blood pressure is -0.11 , and with drop is 0.26 . The multiple correlation of both with outcome is 0.27 and this is statistically significant. It has recently been pointed out that the Funkenstein curve tends to change with age, and it has been suggested that its relation with outcome after treatment is essentially a function of age. I have found that the addition of age to the multiple correlation raises it to 0.28 , a negligible increase. Thus the Funkenstein test is providing information which is independent of age. By itself, age has a correlation of 0.10 with outcome after treatment.

It has been possible to quantify the relationship between outcome after treatment and the Funkenstein test and other variables, because we have been using a specially devised rating scale which contains 17 variables. The inter-correlations between these variables have been calculated and latent roots and vectors obtained. The first vector (factor) corresponds fairly obviously with that of endogenous depression. The second corresponds, but not so well, with that of reactive depression. (It must be remembered that factors can never truly correspond with diagnostic categories.) The third factor does not correspond with any recognizable clinical syndrome, but it does have significant correlation with outcome, and it is the only one that has. The fourth factor does not correspond with any obvious clinical

syndrome, but on investigating the case histories of those patients who score high in this factor, it is seen that they have abnormal, inadequate, asocial personalities. (At this point three typical case histories were reported.)

The relation between outcome after treatment and factor measurement is as follows: F_1 0.23, F_2 0.17, F_3 0.27, F_4 -0.09. The five highest correlations between outcome and variables investigated are as follows: Length of history 0.46, weight -0.31, body index (Rees-Eysenck) 0.29, the initial score on rating scale 0.28, Funkenstein drop 0.26. These are not high, but in view of the smallness of the inter-correlations, it is not surprising that the multiple correlation between these five variables and outcome after treatment is 0.62. This is about as high as is ever obtained in the field of research on personality, although it must be pointed out that it is not very helpful for prediction of the outcome for any individual patient.

The results obtained so far are interesting, but need to be interpreted with caution. The correlation between the variables investigated and outcome after treatment is low, but this is due partly to the careful selection of patients and partly to the post-treatment fluctuations of the patients' condition. The problem of relapses and recurrences is clearly related to that of giving an appropriate dose of E.C.T., and until this problem is settled little further increase in these correlations is to be expected. It is of interest that three of the "predictor" variables are concerned with physiological and constitutional measurements.

The quantitative assessment of the Funkenstein test shows that its relation to outcome is small. The test is of little practical value at the moment, but it is of considerable theoretical interest and needs further development.

This investigation can be summarized as follows: the Funkenstein test has been dissected into reliable and unreliable variables and the former have been proved to show a relation to outcome, albeit a small one. The use of a specially designed rating scale has given quantified relationships with outcome, and also suggested that a particular group of symptoms is related to an abnormal type of personality. Finally, the multiple correlation with outcome has indicated the importance of constitutional factors.

REFERENCES

- FUNKENSTEIN, D. H., GREENBLATT, M., and SOLOMON, H. C. (1952) *Psychosom. Med.*, **14**, 347.
 GELLHORN, E. (1953) *Physiologic Foundations of Neurology and Psychiatry*. Minneapolis.
 MUNRO, D. E. (1958) M.D. Thesis, Glasgow (unpublished).

Dr. C. M. B. Pare (London):

Iproniazid in the Treatment of Depression

Much of the interest in iproniazid stems from the fact that its use in the treatment of depression followed logically from data acquired from animal experimentation.

In the experimental animal it has been shown that changes in the brain concentration of 5-hydroxytryptamine (5-HT) and catechol amines are associated with alterations in the behaviour of the animal. Thus, the decrease in brain concentrations of these substances obtained after treatment with reserpine results in behaviour compatible with a state of depression (Brodie *et al.*, 1955; Carlsson *et al.*, 1958) whilst an increase, obtained by administration of a precursor substance, leads to excitement (Bogdanski *et al.*, 1958; Carlsson *et al.*, 1958). Iproniazid has a marked inhibitory effect on mono-amine oxidase, the enzyme largely responsible for the inactivation of 5-HT (Sjoerdsma *et al.*, 1955). A proportion of the naturally occurring catechol amines are also inactivated by this mechanism (Leeper *et al.*, 1958). By virtue of this action on mono-amine oxidase, iproniazid leads to increased brain concentrations of 5-HT and catechol amines and again this is associated with a state of excitement (Spector *et al.*, 1958).

In man, reserpine has a tendency to induce a state of depression and also liberates 5-HT from its binding sites in platelets (Carlsson *et al.*, 1957) although there have been no direct observations on brain tissue. Conversely, iproniazid, which may cause euphoria, gives rise to increased concentrations of 5-HT in human platelets (Pletscher and Bernstein, 1958).

Although there is no evidence to suggest that the depressive illnesses seen in clinical practice are due to a deficiency of 5-HT or catechol amines, it is not unreasonable to postulate that any improvement obtained with iproniazid may be connected with altered concentrations of these substances. The present investigation was, therefore, designed to answer the following questions: (1) Does iproniazid benefit patients with depression? (2) If so, can the patients who respond be differentiated clinically or biochemically from those who do not? (3) In patients who respond to iproniazid, is the benefit due to changes in the concentrations in the brain of 5-HT or of catechol amines?

Method.—50 patients with depression who had been considered suitable for E.C.T. were given iproniazid in doses up to 450 mg./day for periods varying from two to forty weeks. Placebo was also used. The degree of depression was assessed by weekly rating scales which were completed by the junior psychiatrist in charge of the case who was unaware when placebo tablets were being

used. Patients were said to respond to iproniazid if the depression improved with treatment, relapsed when placebo was substituted and improved again when iproniazid was reintroduced. Patients who improved with iproniazid but did not relapse when placebo was substituted had necessarily to be designated as "coincidental" improvement.

This method, unsatisfactory from some points of view, was sufficiently elastic for use with a new drug where such things as dosage and the time elapsing prior to any improvement were insufficiently known. More important, it ensured the selection of a group of patients known to respond to iproniazid and equally important, a group who, because of a prolonged course of treatment, could be definitely assessed as having failed to respond.

Results.—(1) *Does iproniazid benefit patients with depression?* The results are shown in Table I. Taking the total number of patients who

| TABLE I.—RESULTS | | | |
|---------------------------------|----|----|----|
| Cases improved | | | 26 |
| Improvement "due to iproniazid" | 12 | | |
| "Coincidental" improvement | 14 | | |
| Cases not improved | | 24 | |

improved, whether "coincidentally" or in "response to iproniazid" the 52% improvement compares closely with that reported by other workers (Symposium on Iproniazid, 1958). The improvement in patients defined as having "responded to iproniazid" usually commenced during the second or third weeks of treatment and this delay was not shortened by increasing the dose of the drug. There appeared to be no advantage in giving iproniazid in doses greater than 200 mg./day. On the other hand, some patients relapsed on dosage lower than 150 mg./day. There was no evidence that iproniazid cuts short a depressive illness, but rather that it provides symptomatic relief for as long as the drug is continued.

(2) *Can the patients who respond be differentiated clinically or biochemically from those who do not?* We were unable to differentiate clinically those patients who would be expected to improve with iproniazid from those who would not. There was a suggestion that patients who "responded to iproniazid" had pre-treatment values for urinary 5-hydroxyindoleacetic acid (5-HIAA) which were lower than those in patients who did not respond (Table II). (For methods see Pare and Sandler, 1959a).

| TABLE II.—SHOWING THE MEAN VALUES FOR URINARY 5-HIAA IN MG/G. CREATININE IN EARLY MORNING SPECIMENS OF URINE COLLECTED PRIOR TO IPRONIAZID THERAPY | | |
|--|------------|--------------|
| | 5-HIAA | |
| 9 patients who improved "due to iproniazid" | 3.0 ± 0.50 | } P = < 0.05 |
| 6 patients who did not improve with iproniazid | 4.5 ± 0.75 | |
| 7 patients who improved "coincidentally" with iproniazid therapy | 3.1 ± 0.86 | } P = > 0.1 |

(3) *In patients who respond to iproniazid, is the benefit due to changes in the concentrations in the brain of 5-HT or of catechol amines?* In animals, 5-hydroxytryptophan (5-HTP) and 3, 4-dihydroxyphenylalanine (DOPA) are known to increase the brain concentrations of 5-HT and catechol amines respectively (Udenfriend *et al.*, 1957; Carlsson *et al.*, 1958).

Patients who were known to "respond to iproniazid" were given DL-5-HTP and DL-DOPA by intravenous injection at intervals of at least a day, at the same time of the day and in random order. Three patients were given the drug in a single dose of 12.5 mg. while receiving iproniazid but during the period of therapy before improvement was expected. Three patients were given the drug in the absence of iproniazid. In this group the dosage ranged from 25 mg. of each drug in a single injection to 150 mg. 5-HTP and 275 mg. DOPA, each over a forty-eight-hour period. Neither clinical nor psychological assessments demonstrated any alleviation of the depression by either drug. In addition, one patient was given 5-HTP and DOPA together, in doses of 12.5 mg. of each subcutaneously twice daily for sixteen days. No improvement in the depression was noted clinically.

Any relief from depression was bought at the price of side-effects which were pronounced and frequent. One patient developed jaundice ten days after stopping iproniazid and died from acute hepatic necrosis thirty-three days after stopping the drug. When we became aware of the danger of liver damage, "standard tests of liver function" were carried out routinely in 24 patients. Serum bilirubin, thymol turbidity, zinc sulphate turbidity, alkaline phosphatase and serum proteins showed no significant abnormality. Serum glutamic-oxalo-acetic transaminase (G.-O.T.) activity, which has recently come into extensive use as an index of hepatocellular damage, was also carried out in 29 patients. (For methods see Pare and Sandler, 1959b.) Values were within normal limits of 8–28 units/ml. at 20° C. in all sera prior to drug treatment. In 9 patients levels above the normal range, up to 140 units/ml., were found during iproniazid administration. On stopping the drug the levels gradually dropped, taking about four to six weeks to return to normal. There did not appear to be any correlation between the dosage or the length of time that the patient had been taking the drug and the rise in serum G.-O.T.

It is now generally accepted that fatal hepatic necrosis is an occasional toxic effect of iproniazid though the true incidence of this complication is unknown. It is in this context that the G.-O.T. findings must be considered. Although the interpretation is difficult, we would suggest that

any rise detected in routine weekly serum G.-O.T. estimations should, in the present state of our knowledge, be treated as presumptive evidence of early liver damage and that the drug be discontinued.

Conclusions.—Perhaps of most interest is the question whether iproniazid is a general euphoriant or whether it acts only on those patients whose depression is due to a specific metabolic abnormality which has yet to be identified. The striking response to iproniazid noted in some patients compared with the apparent ineffectiveness of the drug in others suggests that the latter may be true. Certainly it did appear that, prior to treatment, there was a lower turnover of 5-hydroxyindole metabolism, as judged by the urinary excretion of 5-HIAA, in patients who subsequently responded to iproniazid, compared with patients who did not respond. On the other hand, neither parenteral 5-HTP nor DOPA, in the dosage used, resulted in any symptomatic improvement and it may be that other amines reported to be affected by mono-amine oxidase inhibitors are of importance (Udenfriend, 1959).

Be that as it may, the present position is that iproniazid is providing an enormous stimulus to the development of a rational chemotherapy of depression. While it is to be hoped that future amine oxidase inhibitors will be free of hepatotoxic effects, the use of iproniazid in clinical prac-

tice should always be carefully considered, and, if used, accompanied by weekly serum G.-O.T. estimations.

Acknowledgment.—This investigation was carried out in conjunction with Dr. M. Sandler, late of the Royal Free Hospital Medical School.

REFERENCES

- BOGDANSKI, D. F., WEISSBACH, H., and UDENFRIEND, S. (1958) *J. Pharmacol.*, **122**, 182.
 BRODIE, B. B., PLETSCHER, A., and SHORE, P. A. (1955) *Science*, **122**, 968.
 CARLSSON, A., LINDQUIST, M., MAGNUSSON, T., and WALDECK, B. (1958) *Science*, **127**, 471.
 —, SHORE, P. A., and BRODIE, B. B. (1957) *J. Pharmacol.*, **120**, 334.
 LEEPER, L. C., WEISSBACH, H., and UDENFRIEND, S. (1958) *Arch. Biochem. Biophys.*, **77**, 417.
 PARE, C. M. B., and SANDLER, M. (1959a) *J. Neurol. Psychiat.* (In press.)
 —, — (1959b) *Lancet*, **i**, 282.
 PLETSCHER, A., and BERNSTEIN, A. (1958) *Nature, Lond.*, **181**, 1133.
 SJOERDAMA, A., SMITH, T. E., STEVENSON, T. D., and UDENFRIEND, S. (1955) *Proc. Soc. exp. Biol. N.Y.*, **89**, 36.
 SPECTOR, S., PROCKOP, D., SHORE, P. A., and BRODIE, B. B. (1958) *Science*, **127**, 704.
 Symposium on Iproniazid (1958) *J. clin. exp. Psychopath.*, suppl. 1, p. 19.
 UDENFRIEND, S. (1959) New York Academy of Sciences' Conference on amine oxidase inhibitors. (In press.)
 —, WEISSBACH, H., and BOGDANSKI, D. F. (1957) *J. biol. Chem.*, **224**, 803.

Meeting
February 10, 1959

The Phobic Anxiety-depersonalization Syndrome [Abridged]

By Professor MARTIN ROTH, F.R.C.P.

Newcastle upon Tyne

Introduction

It is traditional to begin papers such as this dealing with depersonalization by paying tribute to the ubiquity and versatility of the phenomenon, citing in illustration the experiences of Wordsworth, Amiel and Charles Morgan and continuing with the depersonalization occurring in schizophrenia, affective disorder, obsessional states, temporal lobe epilepsy, head injury, encephalitis, carbon monoxide poisoning, hashish intoxication and botulism. Although all such experiences and observations must be taken into consideration in any examination of the psychopathology of the phenomenon, such a list is somewhat misleading. A fleeting depersonalization is a common and perhaps a universal experience; it is a persistent and intractable change in the experience of the self or the outer world that presents the psychiatrist with such baffling problems. Further, such a list appears to confer an equal status to the very rare and the

commonplace. And a similar one could be compiled for the majority of entities known to psychiatry, certainly hysteria, anxiety state, obsessional disorder and endogenous depression.

The great majority of cases of depersonalization seen in everyday psychiatric practice are neither caused by a gross cerebral lesion nor found in the setting of any constitution as specific as that of the schizophrenic or manic-depressive. There is much evidence to suggest that cerebral mechanisms as subtle, elusive and yet as commonplace as those underlying neurotic disorders are likely to be at work. The investigations which are the subject of this paper were prompted by studies some years ago of a succession of 4 cases, in each of which a chronic neurosis with prominent depersonalization followed a sudden calamity. One of these will now be described.

An attractive, lively but naïve and emotionally-immature girl was prevailed upon by her masterful, domineering mother to break her engagement with

a gentle and taciturn clergyman on account of his poor financial prospects and unimpressive personality. For a month thereafter she was tense, mildly depressed, restless at night and lacking in concentration at her work. At this time, the home being crowded with visitors one week-end, the girl was asked to share a bed with her aunt. During the night she awoke to find her aunt, who was aged 60, dead beside her. Her memory for the subsequent three to four hours was hazy, but according to her parents, she rushed about the house in uncontrollable terror and excitement, complained that she could not see, implored her parents to switch on the lights which were fully lit, pinched herself all over, shouting in a frenzied way that she was numb and dead, and asked others to stick pins into her to assure her she was alive. After she had been sedated and put to bed, she insisted that her breathing and heart beat were about to stop and proceeded deliberately to breathe in and out keeping her finger constantly on her pulse. For two to three days there were periods of excitement in which she ran berserk destroying whatever she could seize. Thereafter the picture, which was to last in chronic form for years, crystallized in complaints that she was dead from the neck down, she felt divided in two, one half was a passive spectator of the other's acts, her movements appeared forced, mechanical, her feelings dead, her thoughts an incessant, tormenting circle of thinking about thinking about thinking. The outside world was covered by a haze, the faces of others seemed twisted and sinister. Her voice sounded as if from afar and she was afraid of looking into the mirror. She complained of a constant feeling of faintness and would not leave the house even if accompanied, nor remain alone in a room. By the time she was admitted to hospital some three to four weeks later, the changes in her body were described in grotesque terms, yet at times with a certain incongruous levity. At night she would require very heavy sedation, having developed a belief of delusional intensity that she would sink to death. Her behaviour was histrionic in the extreme and she would cling importunately to doctors and nurses. The diagnosis offered certain obvious difficulties yet for much of the time the patient was like many other cases of florid depersonalization. Within a month, the quasi-delusional ideas had resolved, all the grotesque complaints being now qualified by an "as if" statement. Within a year, recovery was complete and over a period of eight years there has been no recurrence of this illness.

Clinical Material

The mode of onset, clinical picture and course pursued by the illness in this case were frequently to recur in our subsequent studies which covered 135 cases. These were compared in respect of 100 items relating to heredity, family background, early development, previous personality, pattern of adjustment and features of the illness with 50 control patients suffering from other neuroses and for relevant items also with 50 individuals who had recently recovered from a

physical illness and had never suffered from a psychiatric disorder. 6 patients in whom the depersonalization was associated with a cerebral lesion and 5 others who had depersonalization in association with an indubitable psychosis of schizophrenic or depressive type are not included in this report.

There were 93 women (mean age 35 years) and 42 men (mean age 38 years). The most common age of onset among women was in the late twenties but there were smaller peaks for age of onset in the late thirties and the latter part of the sixth decade. The concentration of cases in early life was much less marked among the men. The neurotic controls consisted of 26 men and 24 women (mean ages 36 and 37 years respectively) and the controls recovering from a physical illness of 21 men and 29 women (mean ages 38 and 35 years).

Precipitating Factors

Over two-thirds were women and, although the commonest age of onset was in the late twenties, there was an unexpectedly high proportion of cases with first breakdown occurring after the age of 45. The association with calamitous circumstances was striking. The illness had frequently followed closely on a bereavement or suddenly developing serious illness in a close relative or friend (37%), illness in, or acute danger to the patient himself (31%) and frequently severance of family ties or acute domestic stress which often constituted a threat to marriage (15%). Thus in 83% of the cases the illness was consequent upon circumstances of a painful, threatening or disastrous nature. In 13% of the women illness commenced during pregnancy or after childbirth; an abrupt onset shortly after delivery accounted for most of the cases in this group. Physical illness was numerically more important among the men and commoner among the older patients and bereavement among the women. Some examples of precipitating events were the girl of 21 (described above) discovering during the night that her aunt was dead in bed beside her, a young mother finding her child in status epilepticus from which she subsequently died, a child of 14 witnessing her father's massive hæmatemesis, a nervous, obsessional workman seeing his mate collapse and die from a coronary thrombosis and finding an hour later the man's false teeth in his pocket. The difference between the phobic anxiety-depersonalization cases and neurotic controls in the total incidence of clear-cut precipitating factors for the illness was statistically significant ($P < 0.01$); so was the incidence of bereavement in both sexes and of physical illness among the men ($P < 0.05$).

Disturbances of Consciousness

There is an interesting association of onset with spontaneous accidental or induced change in consciousness, often of a slight or transient character. 12% of the illnesses were initiated in this way, not including the anaesthesia of childbirth. 6.7%, mainly in young men and women, were initiated by a sudden, unexplained syncopal attack, almost invariably followed by a fear-laden preoccupation with the possibility of fainting again, and usually an intense phobic aversion to leaving home, as well as depersonalization. In 3 of these patients consciousness had been lost on more than one occasion and in 2 of them convulsive movements had been observed during the attacks, although these had the unmistakable characteristics of syncope in that dimness of vision, feelings of faintness and loss of equilibrium preceded the loss of consciousness. A diagnosis of temporal lobe epilepsy had been previously made in 2 of these cases, yet the EEG was in each instance normal and attacks had been confined to the first few months following the onset of the disorder and, in the 6 patients whose illness had been in progress for a number of years, there had been complaints of faintness or "giddiness" but no further loss of consciousness. None of these patients is at present on anti-convulsant medication. A third of the cases suffered during the chronic phase of the disorder from feelings of faintness or unsteadiness, the difference from neurotic controls being statistically significant (males $P < 0.01$, females $P < 0.05$).

There are other observations to suggest that the cerebral mechanisms concerned with the regulation of awareness may have some special significance for the physiopathology of the phenomenon. Thus one patient of 59 suffered a third attack of pneumonia. Following two previous attacks, ten and fifteen years earlier, he had been wildly delirious and during one of these bouts had run berserk and destroyed much of the furniture in the room where he was being nursed. He could remember nothing of these happenings. During the third attack, for which he was given antibiotics, there was no frank delirium, but he was drowsy, hazy in thought, inattentive, and experienced a constant distortion of visual perception, the furniture appearing constantly to change in shape, and walls and ceiling to undergo a pulsating movement advancing towards and receding from him. A severe phobic anxiety and depersonalization merged insensibly with these experiences.

Moreover, in 11.8% of cases a brief period of clouding of consciousness had occurred at some stage of the disorder, in most instances at the commencement of the illness, immediately after

the impact of the acute trauma. One patient became stuporous and another, after being told he looked dreadfully ill, became disorientated, incoherent in speech and finally violently aggressive. He remained clouded for twenty-four hours and was subsequently completely amnesic for this period. In a number of cases, after a period of diffuse anxiety there was an interval of hours or days following the acute trauma and the depersonalization began after a sudden start from half-sleep usually preceded by a vague awareness of palpitations or some other bodily discomfort. For a long period thereafter these patients would fear going to sleep lest they sank to death and surges of panic when on the point of losing consciousness were common. Although these cases form only a small proportion of the total material, in precipitating factors, subsequent course and premorbid personality they manifest no clear differences from the remaining cases.

Depersonalization and Phobic Anxiety

There were the usual distressing feelings of change in the self, of negative transfiguration of the outer world, commonly with a compelling self-scrutiny and an oppressive sense of loss of spontaneity in movement, thought and feeling.

This loss of spontaneity led to the patients' complaints that activities no longer flowed from them unawares, as it were; they were compelled to scrutinize each thought, act and emotion in its detailed development. There was an associated subjective experience of automaton-like behaviour and of being a passive spectator of the activities in which the self was engaged. The impression conveyed by these subjective descriptions was that of an awareness suspended somewhere midway between the levels of nervous function appropriate to voluntary and automatic or secondarily automatized activities.

Only passing mention can be made of the subjective experiences of bodily changes—the torso transmuted to marble, the head, in one case, "inflated with cold air like a balloon", the hands enlarged and dead in the mornings, "the fingers just strings of sausages", the illusion of a change in shape (rendered by an intelligent patient in helpless perplexity, "I have been transformed into an object with square outlines"). Just under half the patients were derealized; the world had become unfamiliar, still, remote. A deadness, unrelenting and ubiquitous, descended upon it. A number of patients complained of an ineffable dread of faces on the television or cinema screen—they had acquired a sinister, evil aspect sometimes associated with an illusion of distortion of mouth, nose or eyes.

The symptoms of depersonalization were

associated with a phobic anxiety which varied in severity but was characteristic and uniform in pattern and invariably present. There was a fearful aversion to leaving familiar surroundings, to walking in the street and to entering shops, travelling in vehicles or visiting cinemas or theatres. Waiting or sitting still in such settings was prone to evoke a sense of impending disaster, acute agitation and flight in panic. There was a fear, confessed with a certain shame, of collapsing before others, losing control, making a scene, of being seen as helpless, foolish and ridiculous. True vertigo was rare, a sense of unsteadiness of the legs, an illusion of walking on shifting ground and a feeling of lightness in the head being the usual pattern. A fear of loss of consciousness was commonly associated. All these symptoms were prone to be exacerbated by proximity to moving objects as in crowds or near vehicles.

An intimate association between this pattern of phobic anxiety and symptoms of depersonalization is indicated by a number of lines of evidence:

(1) In a proportion of patients, depersonalization which had been present in the early stages of the illness subsided to leave this type of phobic anxiety as the only disability.

(2) In many patients with this kind of phobic anxiety depersonalization supervened spontaneously or after a further acute emotional stress.

(3) In a number of patients with this type of phobic anxiety severe depersonalization developed abruptly after the administration of convulsive treatment.

(4) In mode of onset, sex distribution, personality pattern and the early manifestations of illness the group of 20 patients with this type of phobic anxiety alone were not distinguishable from patients in whom these symptoms were consistently or intermittently associated with depersonalization.

(5) In 5 cases with a chronic cerebral lesion in the temporal lobes and persistent depersonalization, an identical pattern of phobic anxiety was found.

Temporal Lobe Features

For these reasons our material of 135 cases includes 20 patients in whom this particular pattern of phobic anxiety has been found without depersonalization.

The association of *déjà vu* experiences and disturbances in the sense of passage of time with depersonalization has often been described. In our material a rich variety of symptoms, in addition to depersonalization which hinted at some subtle disturbance in the function of the temporal lobes or limbic system, was elicited in 37% of cases but in none of the neurotic

controls. These symptoms included the experience of panoramic memory, distortions of perception such as micropsia and metamorphosis, objects in the outside world appearing frighteningly large, or the distinction between foreground and distance being strangely altered. In a few cases there were auditory hallucinations with insight and two patients described olfactory hallucinations, one of these perceiving during attacks the smell of the "lilies of the valley" talcum powder that had been used by his mother who had died of a carcinoma of the breast. Other symptoms were hyperacusis and acute autonomic disturbances occurring, in some instances, during short-lived, sharply-defined exacerbations of depersonalization, associated with a sense of inexpressible dread or horror, and probably a slight dimming of awareness. Time passed quickly or slowly, the past or future seemed remote or the patient might feel himself outside of time altogether. One patient experienced on four occasions an autoscopic hallucination, observing himself walking down the street in broad daylight. Another described attacks in which people would change into animals as he looked at them. 15% of our cases experienced the "private cinema" phenomenon; the patient on closing his eyes in the awake state seeing lattices, flashes of light, stars and spirals which might take shape as an ever-moving succession of objects, animals or faces as if an endless film strip were being projected before him. This phenomenon has been described in pre-delirious and subacute delirious states as also after administration of hallucinogenic drugs and may have some bearing upon the aetiology of the syndrome.

A Pan-neurosis

Hysterical symptoms such as numbness, loss of use of limbs, aphonia, globus hystericus, a coarse generalized tremor or dimness of vision are relatively common in the acute phase of the illness and may be seen during the chronic stage of the disorder (Shorvon, 1946). The incidence of such features was 26%, but had we included all instances of histrionic, importunate behaviour and the strange, incongruous levity with which many patients describe their sufferings, the proportion would have been higher. Other features commonly present were vasomotor disturbances with epigastric discomfort, palpitations, diarrhoea, headache and insomnia (74%), mild obsessional symptoms usually of a ruminative kind and rarely to the forefront of the clinical picture (66%), a hypochondriacal self-scrutiny and preoccupation (45%) and a variable depressive colouring (53.8%), usually in the form of a labile, brooding gloom reminiscent of

reactive depression but giving rise to difficulties in diagnosis, particularly in the older patients. In the latter, the abrupt step-like onset of the illness often for the first time in the life of the patient, the intensity of the depression with frequent suicidal ruminations and some attempts, and the extreme agitation and restlessness in some cases, all contributed to create a close resemblance to endogenous depression. Yet the association with this condition is rare. E.C.T. had been administered in 24 of the cases and with one exception the benefit proved transient and was confined to the depression. The depersonalization and phobic features were exacerbated in the majority of cases and unaffected in the others. Moreover, fluctuations were frequently observed and, at times, readily induced by means of drugs in the depressive symptoms, hysterical features, vasomotor disturbances and hypochondriacal preoccupations without corresponding change in the phobic anxiety or depersonalization, whereas recovery or amelioration of the latter was associated with corresponding changes in the neurosis as a whole.

Psychotic Features

Included in this material are 5 cases who have each had a short-lived psychotic episode with features such as paranoid delusions, auditory hallucinations and, in one instance, ideas of influence that raised a suspicion of schizophrenia. We have felt justified in including these cases as probable variants of the syndrome for the following reasons. In each instance the illness had begun as in the other cases, the trauma in this group being of a particularly painful and distressing nature. The psychotic features subsided within a matter of weeks, the clinical picture returning to the pan-neurosis dominated by depersonalization and phobias which had preceded it, except in the one case in which the psychosis ushered in the illness and receded to reveal this picture. The symptomatology was florid and in all but one case some dimming of consciousness was present at some stage. Good rapport was invariable even in a terrified, hallucinated and perplexed child of 14 whose first attack had commenced after a visit to her father's grave. During the psychotic phase the symptoms of depersonalization assumed an indubitably delusional form but when it had receded the identical distortion in the subjective experience of the self and outside world were complained of, now qualified by "as if" statements.

For these and other reasons that there is no time to discuss here, I suspect we are dealing in this group of cases with a phenomenon which belongs to the interesting area that is becoming

differentiated at the peripheries of schizophrenia and is occupied by such conditions as the short-lived psychoses of battle stress, the oneiroid states, the psychogenic psychoses, some of the phenomena induced by hallucinogenic drugs. I would suspect also that a phenomenon closely similar to the whole phobic anxiety-depersonalization syndrome is classified under the heading of "pseudo-neurotic schizophrenia" in North America (Hoch and Polatin, 1949), an inveterate neurosis in the description of which phobias and depersonalization are mentioned and intermittent psychotic episodes are said to occur. If our analysis of the symptomatology of these cases should prove the correct one, a more appropriate title would perhaps be "pseudo-schizophrenic neurosis".

Family Background and Development

A family history of clear-cut neurotic breakdown in first degree relations was given by 21.4% of patients under the age of 35 and in only 4.9% of those over this age. 5.9% and 3.3% of these groups respectively gave a history of psychosis in first degree relations. These figures are considerably in excess of those obtained for the control groups and although a first comparison of these crude percentages does not yield statistically significant results, the figures are clearly worthy of more detailed analysis. It is of interest that the males proved to be a constitutionally more abnormal group by this as well as by a number of other criteria; the old were likewise less abnormal than the young in this and in other respects. We have been unable to confirm the findings of Wittels (1940) and Shorvon (1946) of a high incidence of disturbed parent-child relations in cases with depersonalization. The findings tended, in fact, to confirm a clinical impression that the patients had come from unusually stable and closely-knit families. The incidence of neurotic traits in childhood was rather higher than in the two control groups and particularly so for mild, long-standing phobias. A relatively common phobia found just as often in cases with depersonalization as in those with phobic anxiety alone was an aversion confined to church or to assembly or prayers at school which seemed to have issued from an experience of faintness or urgency of micturition in one of these settings. The aversion had caused little disability and had remained well encapsulated until the eruption of the full neurotic illness in late adult life. Ill-health in childhood had been present in about a fifth of the cases, the males showing a slightly higher incidence. The neurotic groups differed from the normal controls but not significantly from each other in this respect. However, an

unstable work record was more than twice as common among the neurotic controls as among the phobic anxiety-depersonalization group which was in accord with other evidence that the latter were a relatively stable group of neurotics. A previous history of a clearly defined neurotic illness was elicited in 16% of cases which was a little lower than in the neurotic controls, a somewhat unexpected finding in view of the relatively high proportion of patients over 35 and substantial numbers beyond their fifties.

Previous Personality

Patients were assessed by means of pre-defined clinical criteria for a number of personality traits. They proved to be more dependent, immature, obsessional and anxiety prone and afflicted with mild, chronic phobias than other neurotics, as well as normal controls, to a statistically significant degree. In shyness and social reserve and emotional lability they differed significantly from the normals but were broadly similar to other neurotics while hysterical traits, particularly among the men, were less common than in other neurotics. Our patients were conscientious and scrupulous individuals, people of order and method, the women regarded by their husbands and families as exemplary mothers and housewives and often by their family doctors as "the last person to be neurotic". They were cautious, inclined to be routine-bound, but rarely to the point of gross inadaptability, and obsessional rituals, compulsive checkings and ruminations were rare. In physique and general appearance they were younger than their years. Their demeanour, emotional expression and judgment were immature. The relationship of the women with their mothers tended to be close, intense and often excluded contact outside the immediate family circle.

An interesting facet of the immaturity was the high incidence (60%) of total frigidity among the women, the difference from normal controls being highly significant ($P < 0.01$) yet investigations revealed that the proportion of women married was significantly greater and of those single, lower, than in the general population of the area of comparable age. Yet the proportion of discordant and failed marriages was surprisingly low. The evidence suggested that these women had sought marriage for security and had striven to maintain their marriage ties. The men for whom marriage could be assumed to constitute an additional burden rather than a haven, proved to be a representative sample of the normal population with regard to their marital status.

Despite certain assets then, the general run of our patients could be regarded as vulnerable

because of their rigidity, dependence, immaturity, their incapacity for adult tenderness and affection and their lives narrowly restricted to the pattern set in their youth. It may be suspected that theirs is a world which is perhaps readily made to appear to be crumbling about them under the threat of death or illness. But there were conspicuous exceptions, mainly among those whose first breakdown had occurred after the forties and who had often successfully shouldered a lifetime of heavy responsibility and much vicissitude without any sign of yielding under the strain. There were mothers who had brought up large families of children and men who had been through heavy action in war—a superintendent and a sergeant of police, each with a record of some distinction.

EEG and Biochemical Observations

In 17 out of 60 patients the EEG was classed as abnormal on account of excess theta activity and, in a few cases, medium voltage delta activity in the temporal and occipital areas. The incidence of abnormal records was not significantly different from that in a control group of 32 patients.

The urinary catechol amines have been estimated in 22 patients by Mr. C. Merrills. The mean levels for adrenaline proved to be 19.3 mg. per twenty-four hours (range 6.5 to 49) and for noradrenaline 41.4 mg. per twenty-four hours (range 9.1 to 84). Eight observations on patients who have completed a course of thiopentone injections revealed no significant change in the adrenaline levels (17.05 mg. per twenty-four hours, range 6.7 to 27) but mean noradrenaline had fallen to 10.7 mg. per twenty-four hours (range 0 to 18.8).

Discussion

We have to consider the possibility that we have collected a large number of cases of hysteria, obsessional states, anxiety neurosis, depression and possibly schizophrenia and from this heterogeneous material fashioned a syndrome using a technique familiarized by Procrustes. Such a criticism is implicit in the viewpoint recently adopted in two interesting papers by Ackner (1954) who considers that depersonalization is always merely one component of one of the accepted forms of psychiatric illness. However, if one group of symptoms is no more than an epiphenomenon of another group, it must be shown to co-vary with the latter. Yet the depressive, hysterical and hypochondriacal features, the psychotic symptoms in the small group of "schizophreniform" cases and even the overt anxiety and vasomotor disturbance were the most labile and variable components

of the clinical picture, frequently undergoing amelioration either spontaneously or in response to treatment without corresponding improvement in the depersonalization and phobic aversions. The results quoted in the cases of the depressive symptoms after convulsive therapy were one example of this trend. On the other hand, when phobias subsided, the remaining symptoms were almost invariably abolished as a whole. It would seem, therefore, that it is the depersonalization and phobic symptoms that constitute the essential core of the illness and the other features, the reactive or secondary phenomena.

That the symptoms we regard as the specific core of the syndrome may occur in association with an indubitable schizophrenic or depressive psychosis, as also other forms of psychiatric illness, is not in doubt. But they are to be found only in a very small proportion of cases of these disorders. And if the depersonalization, for example, is at all prominent, it almost invariably resists the treatments to which the remaining symptoms frequently respond. If the existence of a fringe of cases in which a given symptom complex was found in association with some other disorder were allowed to call into question the claims as to independent nosological status of the former, few entities known to psychiatry or, for that matter, to medicine, would survive the test.

As far as precipitating factors are concerned the general consensus of psychiatric opinion is that, as the last of a succession of stresses each of which impinges upon everyone at some time or another, they may be dismissed as playing an insignificant part in the causation of neurotic disorders. There are three unvalidated assumptions implicit in the view that the stresses associated with the onset of a neurotic disorder are of a commonplace kind: (1) that the response of the normal population to stresses such as those described above, for example, is known, (2) that the general run of individuals may be assumed to surmount them without ill-effects, and (3) that the premorbid powers of adaptation of an individual suffering from a neurotic breakdown may be reliably assessed. These assumptions, whose validity is in each case open to doubt, have the effect of directing psychiatric enquiry mainly towards the individual's susceptibilities and defences and the early influences that have shaped them, largely to the exclusion of the immediate causes of the illness and its detailed symptomatology. Yet objective and reliable information is rarely to be had about the former, more readily elicited in the latter.

The neglect of the study of the precipitating factors in neurotic illness is all the more surprising in that the association between acute

fear and neurotic breakdown in times of war is well recognized and particularly illuminating and important observations on the so-called "fright" neuroses were recorded by German authors such as Bonhoeffer (1911), Gaupp (1911), Kretschmer (1917), Wetzel (1921), Kleist (1934) and Kardiner (1941), based on experiences during the First World War. These observations were extended during the Second World War (Grinker and Spiegel, 1945; Sargant and Slater, 1940; Sargant, 1957).

The reason why the knowledge thus accumulated has made so little impression on the theory and practice of psychiatry in peacetime is to be sought, I believe, in the views that have been expressed among others by Kardiner about the specificity of the neuroses of war and Kretschmer in relation to the duration of the "fright" neurosis and its relationship to "hysteria". The former held that conditions of modern warfare gave rise to unique patterns of neurosis normally produced in peacetime only during vast calamity situations such as earthquakes and tidal waves. And yet many of our patients had experienced stresses that must have been comparable in severity with those prevalent in times of war and which had, moreover, a close and impressive association with the onset of their neurotic illness. Kretschmer held that the "fright" neurosis was always an evanescent phenomenon. The reasons for its chronic perpetuation were to be sought in the insinuation of a wish, of a desire to escape into illness. This would throw the main burden of causation in chronic cases upon the previous personality and its unconscious needs and desires which the stress at onset had served merely to reveal. However, studies of the long-term course of the traumatic neuroses of war have been few and far between and there would appear to be little objective evidence that all chronicity can be thus assumed to be "motivated" or "hysterical". In our cases while half-conscious appeal for sustenance and support and a desire to perpetuate a dependent role were possible factors in chronicity in a very few cases, they seemed very unlikely to play a part in many more. One wonders how much views such as Kretschmer's owed to the ever-present emotional conflicts and the complications introduced by pension claims which are so prone to obfuscate considerations of aetiology in times of war.

The resemblance between the syndrome we have studied which almost invariably presents in the chronic stage and the illness described in the available literature on the chronic stage of the neuroses initiated by overwhelming fear seems to me to be suggestive. Although the disorders are described in Kardiner's account under such headings as hypochondriasis, transference

neurosis, defensive ceremonials, psychosomatic disorders, sensorimotor disorders and "acute shock psychosis and the epileptic symptom complex", there are certain features which transcend the different categories and with which we have become very familiar: the syncopal attacks with fear of losing consciousness, the anxiety about falling asleep, the terrified starts from slumber, the phenomena strongly reminiscent of temporal lobe dysfunction, the hysterical and obsessional features, the phobias and symptoms suggestive of depersonalization. The cases also have in common the transient stage of clouding of consciousness after the impact of stress in a proportion of cases.

There are obvious difficulties in the interpretation of what constitutes stress. But from the consistencies in the character of the precipitating factors, the immediate and impressive psychological effects they produce, the clear differences in these respects from other neuroses and the similarities discussed above we have concluded that the stresses at onset must play a part in the causation of the illness that follows. However, in a small proportion, the phobic anxiety-depersonalization commences spontaneously or after an unexplained syncopal attack. Moreover the stresses impinge upon individuals who are dependent, inflexible and immature and had possibly been conditioned to respond in an exaggerated way to situations of a fearful and calamitous nature. This is clearly part of the explanation for the overwhelming effect they exert. But here again there were many, particularly among the older patients, in whom investigations failed to reveal such Achilles' heels. In either case the clinical picture is the same. We deal not with a graded affective response, but with a phenomenon that has "all or none" characteristics. Moreover, neither calamities nor dependence, immaturity, rigidity and their psychological antecedents, clearly relevant as they are, can wholly explain an illness of which depersonalization, *déjà vu* phenomena, syncopal attacks and phobias are features. There is a gap which psychological explanations cannot bridge.

The only ways we have at our disposal for evoking depersonalization at will, namely, the administration of hallucinogenic drugs and the stimulation of the temporal cortex, involve an indubitable change in the level of awareness, yet one so subtle that some of the experiences are often registered and retained and subsequently recalled. And as in the phobic anxiety-depersonalization syndrome, we deal with phenomena that may run the whole gamut of temporal lobe symptomatology and are associated with disturbances in the integration of

perception, emotion and the temporal sequence of events and involve in addition a small hazard of loss of consciousness, it seems likely that we are dealing with some chronic derangement of the mechanisms regulating awareness; in these states we are concerned with one of those step-like arrests of arousal with which we are familiar at deeper levels in the patterns of delirium and irreversible coma. This hypothesis, crude though it is, has the merit of meaningfully linking with the three main modes of onset defined in this condition: calamity, acute physical illness and the exhaustion or anaesthesia associated with childbirth. A number of other observations fall into place: the frequent feelings of faintness and the syncopal attacks, the acute psychotic episodes often with clouding of the sensorium now seen as having affinities with the short-lived "schizophrenias" of battle stress.

Depersonalization or dissociation of consciousness which often attends acute stress may be suspected as playing a purposive role when short-lived in that it probably helps to prevent the individual from being overwhelmed by emotion. In the light of the foregoing discussion, the neurosis we have described may be viewed biologically as the maladaptive prolongation of a protective response.

Summary

A new form of neurotic illness is described. Its most consistent features are a combination of depersonalization and a characteristic form of phobic anxiety, but in 40% of cases there are other features reminiscent of disturbances of temporal lobe function such as *déjà vu* phenomena, metamorphopsia and panoramic memory and, in a higher proportion, more variable obsessional, hysterical, depressive features and vasomotor disturbances. In a few cases, short-lived episodes have been observed.

In a high proportion of cases the illness follows upon a calamity or acute physical illness, the incidence of such specific precipitants being significantly different from that in a control group of neurotics. The patients are dependent and immature but also scrupulous, fastidious and inflexible; they differ significantly in these respects from other neurotics and from normal controls, but observed differences are based largely on clinical studies at the present time. The EEG does not differ significantly from that in control cases but preliminary studies reveal a sharp fall in urinary noradrenaline following a course of thiopentone injections. Reasons are adduced for concluding that the calamitous situations at onset play some part in causation. They impinge upon personalities that are predisposed to respond in an exaggerated way

to such stresses, but it is considered that motivation in the ordinary sense cannot explain the chronicity of the majority of these cases, nor the stamp of a subtle cerebral disorder which is characteristic of them. Certain features suggest that a subtle, sustained disturbance in the function of the temporal lobes or limbic system may be involved in the perpetuation of the phenomenon.

REFERENCES

- ACKNER, B. (1954) *J. ment. Sci.*, **100**, 838.
 BONHOEFFER, K. (1911) *Allg. Z. Psychiat.*, **68**, 371.
 GAUPP, R. (1911) *Z. ges. Neurol. Psychiat.*, **5**, 457.
 GRINKER, R. R., and SPIEGEL, J. P. (1945) *War Neuroses*. Philadelphia.
 HOCH, P., and POLATIN, P. (1949) *Psychiat. Quart.*, **23**, 248.
 KARDINER, A. (1941) *Psychosom. Med. Monogr. Suppl.*, II-III.
 KLEIST, K. (1934) *Kriegsverletzungen des Gehirns*. Leipzig.
 KRETSCHMER, E. (1917) *Z. ges. Neurol. Psychiat.*, **37**, 64.
 SARGANT, W. (1957) *Battle for the Mind*. London.
 —, and SLATER, E. (1940) *Lancet*, ii, 1.
 SHORVON, H. J. (1946) *Proc. R. Soc. Med.*, **39**, 779.
 WETZEL, A. (1921) *Z. ges. Neurol. Psychiat.*, **65**, 288.
 WITTELS, F. (1940) *Psychoanal. Rev.*, **27**, 57.

Thiopentone Treatment of the Phobic Anxiety-depersonalization Syndrome

A Preliminary Report [Abridged]

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This paper is concerned with the results of a controlled trial of a form of treatment adapted from Pentothal abreaction (Sargant and Slater, 1940; Shorvon, 1946). It was observed by Professor Roth that a series of 10 to 12 Pentothal injections administered three times weekly brought about a cumulative relief in the tension and depersonalization, even when no abreaction had taken place. A form of thiopentone sleep treatment was therefore developed, in the course of which 2.5% solution is injected at a rate sufficient to induce light sleep in about fifteen minutes. Discussion with the patient is confined to simple explanation and reassurance during the stage of induction. The injections are given on alternate days and in patients who respond improvement generally begins after three to four treatments and continues during the remainder of the course, and in many cases after its termination. It is of interest that prior to the amelioration in psychiatric symptoms, an improvement in the patient's complexion and general appearance and well-being, reminiscent of that seen in the course of E.C.T., is often observed.

Of a preliminary series of 32 patients, many of whom were chronic invalids, 16 became largely or wholly symptom free after a course of this treatment, and 9 were improved. One patient, who had been completely housebound and oppressed by feelings of depression for ten years, lost her symptoms and resumed a perfectly normal life. A controlled trial was instituted following these observations. Cases were allocated at random so that 50% received a course of thiopentone treatment, 25% had placebo injections and 25% had psychotherapy. Before

treatment each patient was graded for severity of central symptoms of depersonalization and phobias, peripheral symptoms such as tension and depression, and degree of incapacity. During follow-up, changes were graded by Professor Roth, who was unaware of the treatment given, and the patient also assessed her overall change. At each follow-up visit psychiatrist's and self-assessments were made on the scale Grade I (recovered or greatly improved); Grade II (improved); Grade III (unchanged).

To date, 44 patients have been followed up at one week and one month, and 28 at three months. At one week, improvement had occurred in a high proportion in all groups, with an excess Grade I improvement in the thiopentone group which did not reach statistical significance. At one month, a Grade I or II improvement by the psychiatrist's grading had occurred in 80% of the thiopentone-treated cases, compared with about 50% in the control groups. Corresponding figures for self-assessment were 90% and 70% respectively. The excess of Grade I results in the thiopentone group, and the overall improvement in this group by self-assessment, reached significance at $P < 0.05$. At three months, improvements in the thiopentone group were maintained, roughly 85% being in Grades I and II compared with less than 50% in the control groups, by both assessments. These differences were significant at $P < 0.05$.

Complete recovery was rare and only one patient achieved the maximum status score at any follow-up assessment. But in many patients the symptoms became mild, fleeting and infrequent, the change had a qualitative stamp, and their lives were transformed by it. A

number of patients housebound over many years were able to resume a relatively normal life. These included only one case treated by psychotherapy.

The quantitative grading necessary for statistical purposes in a controlled trial conceals many qualitative differences between groups. In this trial it was noticeable that patients in different groups improved in different ways. When depersonalization and phobic symptoms cleared rapidly, there was some immediate corresponding improvement in depression, anxiety, and hypochondriasis, but such peripheral symptoms showed a progressive amelioration in the subsequent three months with corresponding improvement in self-confidence. After psychotherapy and placebo, on the other hand, improvement was nearly always confined to peripheral symptoms, depersonalization and phobias persisting, and with one exception substantial improvement after psychotherapy was shortlived. For a time these patients felt less tense and seemed less distressed by, and more able to accept, their unreality feelings, but even peripheral symptoms such as depression, tension, and hypochondriacal self-scrutiny generally returned within a few weeks. Needless to say we were attempting to control the effect exerted by a course of 10 psychotherapeutic interviews, and not evaluating the full contribution that can be made by psychotherapy in this disorder.

Discussion

Since it is notoriously difficult to assess the value of a new treatment in neurosis, this trial must, at the present stage, be interpreted with reserve. But the figure of 85% improvement is certainly encouraging, particularly in relation to a condition that is generally considered to resist other treatments in a high proportion of cases.

We may then tentatively conclude that an accumulative amelioration of symptoms is effected by this form of treatment that is to some extent independent of the effects of psychological intervention, and must in part be attributable to the pharmacologically induced alterations of consciousness. Even a transient qualitative effect such as this upon the central features of a specific neurosis would be of some theoretical interest. However, the improvement initiated by thiopentone in some cases augments afterwards and in the majority seems self-perpetuating for at least three months.

In recent years, application of learning theory to the problems of neurosis has led some workers to propose explanations for the mode of action of certain drugs. However, if the effect of barbiturates is to increase extraversion by altering the strength of inhibition in the cerebral

cortex, "dysthymic" symptoms such as phobias and anxiety, and dissociative symptoms such as faints and depersonalization, ought to be affected in opposite directions (Eysenck, 1955, 1957a, b); an amelioration covering both groups of symptoms is difficult to explain. As the situations for which there were phobic aversions were not evoked or discussed, it is difficult to attribute the improvement to reciprocal inhibition of neurotic responses (Wolpe, 1958). There are obviously difficulties about accepting for our procedure the explanations put forward by Sargant and Shorvon (1945) for the efficacy of Pentothal abreaction.

It seems well established that thiopentone alters consciousness by inhibiting the reticular arousal system (French *et al.*, 1953) and it is of considerable interest that Rothballer (1956) has identified a nor-adrenergic component in this system. It would seem also that noradrenaline is antagonized by thiopentone (Adriani and Roventine, 1941; Dundee, 1956). The possibility therefore arises that the treatment we have described owes its effect to the changes that it induces in the brain-stem in virtue of these properties of thiopentone. Some support for this suggestion is provided by the observation in our preliminary studies that the level of urinary noradrenaline falls sharply after the completion of a course of thiopentone treatment.

The investigation of the effects of empirical physical treatments might well prove a fruitful approach to the identification of causes in neurotic illness; this requires the formulation of hypotheses susceptible to experimental validation. In the further investigation of the form of treatment described here, detailed studies of effects on catechol amine metabolism and the electrophysiology of the brain seem indicated.

REFERENCES

- ADRIANI, J., and ROVENTINE, E. A. (1941) *Anesthesiology*, **4**, 253.
DUNDEE, J. W. (1956) Thiopentone and Other Thiobarbiturates. Edinburgh.
EYSENCK, H. J. (1955) *J. ment. Sci.*, **101**, 28.
— (1957a) *J. ment. Sci.*, **103**, 119.
— (1957b) *A Dynamic Theory of Anxiety and Hysteria*. London.
FRENCH, J. D., VERZEANO, M., and MAGOUN, H. W. (1953) *Arch. Neurol. Psychiat.*, Chicago, **69**, 519.
ROTHBALLER, A. B. (1956) *Electroenceph. clin. Neurophysiol.*, **8**, 603.
SARGANT, W., and SHORVON, H. J. (1945) *Arch. Neurol. Psychiat.*, Chicago, **54**, 231.
—, and SLATER, E. (1940) *Lancet*, ii, 1.
SHORVON, H. J. (1946) *Proc. R. Soc. Med.*, **39**, 779.
WOLPE, J. (1958) *Psychotherapy by Reciprocal Inhibition*. Stanford.



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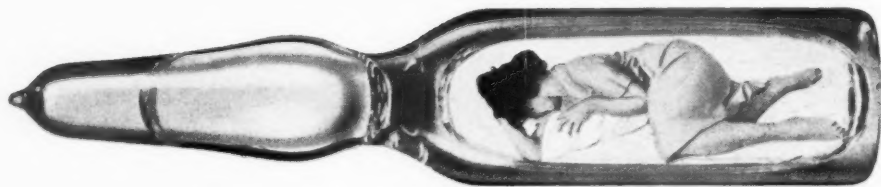
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President—ROBERT COOKE, Ch.M.

Meeting

February 4, 1959

Mr. ROBERT COOKE delivered his Presidential Address entitled **Craftsmanship**.

Meeting

March 4, 1959

Surgical Replacement of the Breast

By Sir HAROLD GILLIES, C.B.E., F.R.C.S.

London

Indication.—Reconstruction of the mammary prominence is indicated after local or radical removal, after atrophy following radiation, or when the gland has failed to develop. It is difficult to appreciate the amount of psychological trauma such a loss entails on the female outlook. Least of all is the surgeon himself apt to be concerned in this aspect of the case. He dreads to amputate but must, and all his life's training and all his skill and ambition lead to the ruthless conquest of the dread disease. Nothing advocated here should for a moment be allowed to interfere with the proper development of the cure by surgery or radiation. The number of mastectomies per annum runs into many thousands.

It can be stressed that the patient is often more concerned with her deformity, which she feels should be remediable, than with the chances of a recurrence over which fate is in control. She will lie to her husband, she will hide her feelings from her surgeon, but to her friend it is the deformity that rends her to cry "I'm ruined".

The extra safety from recurrence that a properly planned plastic will give has argument in its favour. By the implantation of new skin there ensues relief of skin tension along the line of the excision scar, and a mobile skin and fat covering in its place. It may be a reasonable presumption that the tight, atrophic, somewhat bloodless skin following some excisions is more prone to a cancerous degeneration than a well-nourished and freely mobile cover. Many patients also complain of pain in the scar and of limitation of movement.

Halsted (1913) first advocated the implant of a split skin graft instead of direct suture. Free whole-thickness grafts (Blair and Brown, 1958) and free lipodermal grafts (Bames, 1953) are noted. Many others have advocated sliding flaps from the neighbourhood. These local flap methods are apt to cause undue tension and

some secondary disfigurement. For mastectomies with local removal of the gland tissue only, the procedure of Cholnoky (1958) is recommended. Though all aim to give the patient something better, none of them provides a worthwhile volume of skin and fat to match the contour of the normal side. When, however, the remaining breast is of extra large dimensions then a pedicle flap can be transferred to build up the missing one on the one hand and reduce the donor breast on the other (Reinhard, 1942; Thorek, 1942). By far the best of these methods has been published by Holdsworth (1956).

When the defect to be covered is large and deep as following radiation necrosis, the whole sound breast may be rotated over the area, as advocated by Sauerbruch (1925) and Whalen (1953). But for conditions less urgent such rotations are contra-indicated as being inadequate and destructive. Large abdominal flaps are carried up by attachment to the forearm (Converse, 1951) and other large abdominal flaps are used by Marino and Coronel (Marino, 1958). These have the merit of introducing new tissues from a distance. In 1920 a tube pedicle was advocated to carry up a slice of skin and fat from the buttock to make a breast (Gillies, 1920).

There remains the tube pedicle formed to carry the circum-umbilical skin and fat, four examples of which are recorded below. Given the necessary time, a natural-looking breast, soft, warm and complete with make-believe nipple, can confidently be proffered.

A surgeon writes "I simply hate removing a woman's breast and the idea of replacing it is most attractive".

Pertinently he asks *Question 1*: "Having told a woman she has (or may have) a growth should one, dare one, wait three weeks before treating it, while the plastic is being got ready?"

Answer is emphatically "No". But the three weeks' interval is reducible to one week by im-

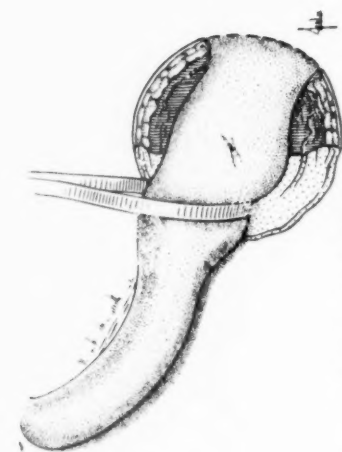


FIG. 2.—Extension of tube leaving 2 in. base. *Wait one week.*

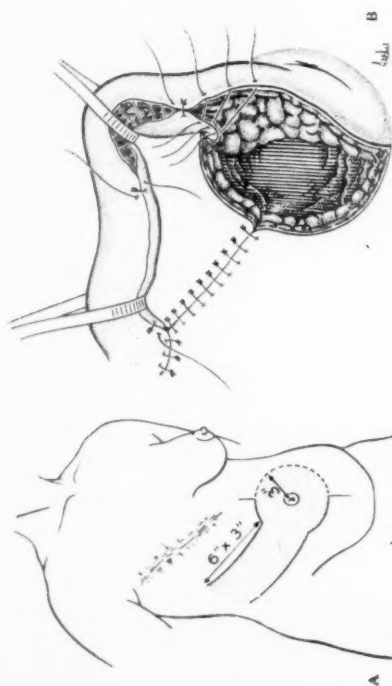


FIG. 1.—A, Plan and incision. B, Pedicle tubed to mid-line. Donor area closed or grafted. *Wait two weeks.*

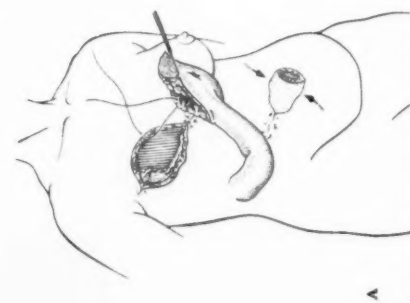


FIG. 3.—A, Freeing of medial end of flap. B, Implantation in mammary position. *Wait three weeks.*

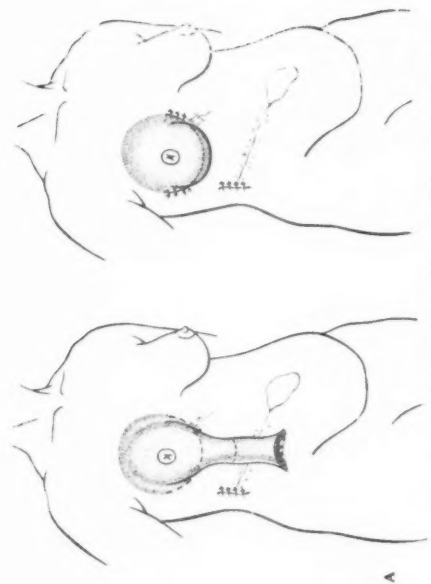


FIG. 4.—A, Division of pedicle. B, Skin and fat fitted in.

provement in technique and by the experience that would follow its wider employment. In particular one already visualizes the addition of a second blood supply to the perimeter of the pancake flap—the part beyond the mid-line and farthest from the point of entrance of the tube pedicle blood supply (Gillies and Millard, 1957). Here it is suggested that either a deep tissue pedicle might prove a satisfactory boost to the blood supply or, more certainly, attachment of the flap to the opposite wrist of the patient. Either of these manoeuvres would allow the pedicle breast flap to be moved with safety after the lapse of one week only.

Question 2: He asks "Could the breast be removed and the pedicle be prepared at the same operation for implant three or four weeks later?"

Answer: "Certainly".

Question 3: "Could one give full X-ray treatment, raise the pedicle at a first operation and at the second remove and replace the breast?"

The answer is "Yes". The influence of the X-rays on the healing of the pedicle skin with that on the margins of the excision would not normally be retarded. Dr. Walter Levitt's communicated view is that if the new breast is implanted in the third week after the X-ray treatment, there might be some mild inflammation along the suture line, but that this would be no contra-indication to the implantation of a healthy flap over the area or to its ultimate success. If further X-ray treatment is required it can be given through the new breast with more safety than over the scar (Fitzgibbon, 1949).

Another question which may well be asked—is this psychological surgery justifiable when the recurrence rate is so high? The answer is that this recurrence rate may possibly be reduced by the treatment advocated and even if a patient has only a five-year expectation of life, that is a long time. Many will have much longer to live (Gordon-Taylor, 1959) and be thankful for a replacement of breast.

The secondary defect and scar on the abdomen have been criticized as a contra-indication. The argument is hardly tenable, for in all cases the abdominal defect at the primary operation or the scar and skin graft at a later stage can be repaired successfully (see Case III, treated by W. G. Holdsworth, my collaborator in this case).

Greater experience in mammary reconstruction and further team co-operation should lead to a considerable improvement in technique. At the moment the ideal is that the patient should leave the table after the mastectomy with the first stage of her new breast in place or in the making. She will never know the horror of asymmetry and will be buoyed up with the presence of a new mammary prominence. She will then gladly

submit at a later date to the rounding off and the finishing of the plastic design. If the start of the repair is delayed, inertia supervenes, the thought of more surgery is unwelcome and the chance to help her may be gone. Sullen acquiescence comes into the picture which the wearing of a "falsie" does little to abate.

Having got the "breast" safely in position there are various minor manoeuvres that will add to its attraction. These can safely be left with the plastic colleague in co-operation. Some of these may be mentioned. The pedicle stump should be denuded of some of its skin and the fat content filled in to raise the contour here or there.

The areola if necessary may be simulated by grafting free whole thickness skin from behind the ear, or if a pinker one is wanted by using the mucous membrane of the buccal cavity. When a browner skin is indicated a part thickness graft may be taken from the opposite normal areola or from the labia minora (Adams, 1949).

The umbilical hollow, if in a good position, may be undermined and projected by implant of cartilage or a plastic prop to simulate the prominent nipple, which like the Tassie that surmounts the Taj Mahal completes the illusion of beauty.

This plea for the replacement of the breast contour after excision is presented for what it is worth to the surgeon and to the patient. It has for its object the removal of the tell-tale scar, a constant reminder of her disaster, and creation of a make-believe substitute which when covered is as good as the "falsie" and when in negligé considerably more appealing.

The technique is illustrated by Figs. 1-4. Total period (minimum) five to six weeks.

CASE REPORTS

Case I (Figs. 5 and 6).—Aged 48. Radical mastectomy (25.1.54).

Pathology.—Typical breast carcinoma. Nodes not involved. No radiotherapy except for keloid at outer end of scar.

1958: No sign of recurrence. Patient complained of deformity and asymmetry of the "horrible holes" above the breast and in the axilla. Patient unable to play tennis or expose herself for swimming. Complained of pain in axilla when writing and a drag on the side as if she were being "pulled down by elastic".

Advice.—Abdominal pedicle flap replacement. Eversion of umbilicus as nipple.

Operation (7.3.58).—Pedicle in right flank 6 in. (15 cm.) long by 3 in. (7.5 cm.) broad, increasing to 3½ in. (9 cm.) at medial end, raised from the deep fascia and the parallel edges sutured together to make a skin tube. The skin of the pedicle was continuous with that surrounding the umbilicus. This area was designed to make a satisfactory volume to match the normal breast and delineated at a 3 in. (7.5 cm.)



FIG. 5A (Case I).—After radical mastectomy.



FIG. 5B (Case I).—After reconstruction by tube pedicle.

radius from the umbilical depression. Wait two weeks.

28.3.58: The side farther from the pedicle was raised down to the deep fascia, the dissection including the freeing of the umbilical hollow. The latter was everted and some fat stitched inside to resemble a nipple. *Note:* As a protruder of the navel skin, something a little firmer is indicated. Cartilage or one of the plastics perhaps at a later stage.

There was the complication of an old appendix scar in the S.W. corner of the new breast. This scar may have had some influence in a slight circulatory failure at the periphery. The unrelieved hæmatoma, however, was much more likely to have been the cause.

11.4.58: Pedicle with "breast" attached swung up and sutured into the normal position after excision of scar tissue. A portion of this scar was sent for histology—the report was negative. It remained to fit in the pedicle which was done on 11.7.58 after an interval made long by the slight complication of the hæmatoma and business reasons.

It was originally intended to carry the pedicle and its fat up to the axilla to fill the hollow caused by the muscle removal. However, the time factor precluded this particular finesse and the patient is content with some minor bunching of the fat and connective tissue under the scar.

A further modelling operation was carried out on 5.3.59. The excessive lower pole was rotated from South to North-east counter-clockwise and sutured there with buried catgut and nylon skin sutures. An



FIG. 6 (Case I).—Navel into nipple. Note appendix scar.

improvement in contour resulted. At the same seance, part of the axillary scar was excised where it was tight and a small Z plastic carried out in relief.

Case II (Fig. 7).—Aged 40.

September 1944: Local right mastectomy in Colombo, included pectoral fascia. Biopsy: Hyperplastic cystic disease (chronic interstitial mastitis).

December 1945: Patient presented herself for examination, complaining of painful scar and deformity. *Advice given:* Excision of scar and implantation of new "breast". *Method:* By tube pedicle carrying circum-umbilical skin and fat pad in stages.

7.2.46: First operation. 22.2.46: Delay operation. 6.3.46: Main operation. Some fat necrosis ensued. Patient sent home to convalescence.

12.7.46: Third operation. Pedicle fitted in. All satisfactory.

24.1.47: *Operation to improve contour:* (1) A dermo-lipomatous graft was padded under the deep



FIG. 7A (Case II).—After radical excision.



FIG. 7B (Case II).—After tube pedicle restoration.



FIG. 7C (Case II).—Profile.

surface of the upper part. (2) A circular mucous-membrane graft from the lower lip was sewn into an area corresponding to the areola as a free graft.

Both operations satisfactory.

August 1959: Very satisfactory and attractive breast.

Case III (Fig. 8).—Aged 18. Referred by Mr. W. G. Holdsworth.

Agenesis of right breast. A nipple was present surrounded by a flat area of brown pigmented skin and many hairs and was 1 cm. higher than the left nipple.

Operations.—27.7.51 (H.D.G. and W.G.H.): Right-sided pedicle to circum-umbilical pad.

20.8.51 (W.G.H.): A delay operation of skin and fat by separation of far edge and folding it under towards its nearer edge. Raw area grafted.

17.9.51: A further delay operation by cutting

across the remaining blood supply from the left side and resuture.

22.10.51, i.e. almost three months after commencement of flap: Pedicle and flap raised and a circular hole made in the flap, to fit over the rudimentary areola.

Despite sporadic staphylococcal infection following hæmatoma the whole procedure was satisfactory and the donor scar was excised by Mr. Holdsworth five years later (3.5.56).

Case IV (Figs. 9 and 10).—Aged 11.

Diagnosis.—Radionecrosis following treatment of a segmental pigmented nævus. The area involved the anterior fold of the left axilla and the whole of the left breast including its skin cover, areola and nipple. The potentialities of a neoplasm supervening were obvious.

Pathological report (Professor W. D. Newcomb, St. Mary's Hospital).—"Warty skin with considerable hyperkeratosis. Dense fibrous scar tissue in dermis with a few dilated blood spaces and many small capillaries."

Plan.—To excise the whole area of affected skin and replace by tube pedicle conveying the circum-umbilical fat. Five stages were needed:

Operation 1 (13.3.42): The tube pedicle was made and, at

Operation 2 (21.4.42), was lengthened across the mid-line.

Operation 3 (12.5.42): The main excision and implant of the new "breast".

Operation 4: Utilization of the fat in the pedicle.

Operation 5: Trim operation and implant of small shaped block of ox cartilage to make prominent the "nipple".

The donor site was covered with Thiersch graft and the scar on the flank, though much stretched, was improved by Z plastics.

3.9.57: The shape of the new "breast" has exceeded expectation. The patient subsequently married and fed her baby who, having expressed his disappointment with the new breast, proceeded to overwork the old.

Acknowledgments are due to my colleagues W. G.



FIG. 8A (Case III).—Unilateral agenesis.



FIG. 8B (Case III).—Tube pedicle embracing areola.



FIG. 8C (Case III).—Reconstruction completed, removal of donor scar.



FIG. 9A (Case IV).—Radio-necrosis, pedicle prepared.



FIG. 9B (Case IV).—Implantation after excision.



FIG. 10 (Case IV).—Left breast reconstructed. Right breast posed after lactation.

Holdsworth, A. J. Evans, Douglas Reid, Halfdan Schjelderup, and many others; to Miss Patricia Archer for the diagrams and to Mr. C. B. Ferrill and Miss N. Walker for their care in the photography of these cases.

Figs. 7A, B and C, and 8A and B are reproduced from Gillies and Millard (1957) by kind permission.

REFERENCES

- ADAMS, W. M. (1949) *Plast. reconstr. Surg.*, **4**, 295.
 BAMES, H. O. (1953) *Plast. reconstr. Surg.*, **11**, 404.
 BLAIR, V. P., and BROWN, J. B. (1958) Quoted by Marino (1958), p. 160.
 CHOLNOKY, T. de (1958) *Surgery*, **44**, 689.
 CONVERSE, J. M. (1951) *Ann. Surg.*, **133**, 95.
 FITZGIBBON, G. M. (1949) *Brit. J. plast. Surg.*, **2**, 13.
 GILLIES, H. D. (1920) *Plastic Surgery of the Face*. Oxford; p. 394.
 —, and MILLARD, D. R. (1957) *Principles and Art of Plastic Surgery*. Boston and London; **1**, 297.
 GORDON-TAYLOR, G. (1959) *Brit. med. J.*, **i**, 455.
 HALSTED, S. W. (1913) *J. Amer. med. Ass.*, **60**, 416.
 — (1924) *Surgical Papers*. Baltimore; **2**, 82.
 HOLDSWORTH, W. G. (1956) *Brit. J. plast. Surg.*, **9**, 161.
 MARINO, H. (1952) *Plast. reconstr. Surg.*, **10**, 204.
 — (1958) *Plásticas Mamarias*. Buenos Aires.
 REINHARD, W. (1942) In: Thorek (1942), p. 385.
 SAUERBRUCH, F. (1925) *Chirurgie der Brustorgane*. Berlin; p. 741.
 THOREK, M. (1942) *Plastic Surgery of the Breast and Abdominal Wall*. Springfield, Ill.
 WHALEN, W. P. (1953) *Plast. reconstr. Surg.*, **12**, 64.
 For further references see Marino (1958).

New Operation for Rectal Prolapse

By Professor CHARLES WELLS, F.R.C.S.

Liverpool

I HAVE traced in the literature between 30 and 50 operations for prolapse of the rectum and would like to add still one more.

Rectosigmoidectomy, the most frequently practised procedure, is followed by relapse in half the cases and by some incontinence in three-quarters of all cases (Thompson, 1950).

True prolapse of the rectum is associated with atrophy of the supporting muscles and ligaments in the pelvis. When the abdomen is opened, the pelvis appears enlarged and empty. The prolapse is only part of a massive sliding hernia in which the peritoneal sac is formed by the rectovesical pouch or by the pouch of Douglas. The rectum is abnormally mobile on a long mesentery. As with all hernia operations, a good result

depends upon the soundness of the repair and peritoneal suture alone is not enough. Attempts have therefore been made to repair the pelvic fascia by direct suture as described by Graham (1942), Goligher (1958) and others. The operation is a difficult one and I have fallen back upon the use of a prosthesis.

Polyvinyl alcohol sponge (Ivalon) was tried out in the dog by my lecturer Theo Schofield at the Mayo Foundation. This substance becomes incorporated into the tissues in which it excites a vigorous fibrotic response, with the production of a firm, almost cartilaginous, mass. I am told that it proved a failure in mammoplasty because it produced, almost literally, marble busts. In the early cases I made a complete tunnel of

Ivalon on the front of the sacrum. We had no trouble, but I became nervous about intestinal obstruction and changed over to an open trough (Fig. 1), which is in any case easier to place in position.

We have done this operation fifteen times—the first five years ago. About half were recurrent cases. The prolapse has been well controlled in every case and all are continent. In two or three women over 70 in whom a separate repair of a vaginal prolapse did not seem justifiable, the standard procedure was carried out for the rectal condition with unexpected and complete relief of the vaginal prolapse as an incidental result. In one patient the abdomen was reopened for another reason several weeks after the repair and complete peritoneal cover of the sponge was observed with no overlying adhesions.

Technique.—The peritoneum on either side of the meso-rectum is reflected laterally as a flap, and the rectum with its superior rectal vessels is lifted forwards from the hollow of the sacrum. The dissection is carried forwards and downwards between the rectum and prostate (or vagina) for about a further 2 in. (5 cm.). A sheet of Ivalon is now attached to the anterior surface of the sacrum between the promontory and the third or fourth segment, by three mid-line sutures of thread. The rectum is then drawn firmly upwards and the Ivalon folded around it to enclose all save the anterior fourth or fifth of its circumference. The Ivalon is attached to the rectum by sutures along the

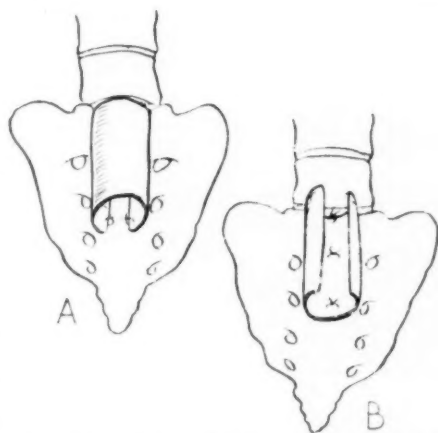


FIG. 1.—A, Sketch of Ivalon sponge attached by its free margins to the hollow of the sacrum to form a tunnel. B, Sketch of Ivalon sponge attached to the hollow of the sacrum to form a trough.

anterior free edge of the sponge. Finally the flaps of peritoneum are replaced to cover the operative field.

(The technique of the operation was illustrated by a cine-film.)

REFERENCES

- GOLIGHER, J. C. (1958) *Brit. J. Surg.*, **92**, 323.
 GRAHAM, R. R. (1942) *Ann. Surg.*, **115**, 1007.
 THOMPSON, H. R. (1950) In: *British Surgical Practice*. Edited by E. Rock Carling and J. Paterson Ross. London; 7, 373.

A Brief Review of Dissecting Aneurysm of the Aorta and a Report of the Successful Treatment of a Case

By A. B. BIRT, F.R.C.S.

Norwich

DISSECTING aneurysm of the aorta has been recognized at autopsy for just over a hundred and fifty years, but it was not until 100 years ago that the first case was correctly diagnosed during life. Shennan of Aberdeen in 1934 in a review of 300 cases from the world literature in the seventy-eight years from 1855 to 1933 found that only 1.6% had been diagnosed before death; but in 1950, Levinson *et al.* reported a series in which 10.6% had been diagnosed during life. The first operative attack on a dissecting aneurysm of the aorta was reported by Gurin *et al.* in 1935, the patient dying of renal failure on the sixth post-operative day. Since then an increasing number of cases has been operated upon, at first without survival for more than a few days, but more recently with an increasing success. As far as I can ascertain from the world literature there have

been 13 successful cases reported: 10 by Creech *et al.* (1956), one by Warren *et al.* (1956) and one by Swann and Bradsher (1956). All these cases were in the United States of America. There is one case from this country (Martin and Muir, 1958) in which operation was temporarily successful but the patient unfortunately died about eight months after operation from rupture of the aneurysmal sac into the pericardium. To these I should like to add my own case of a patient who was operated upon on November 4, 1956, and is still alive and well.

Increased success in surgical treatment entirely depends upon more accurate diagnosis and this will only be achieved if the possible presence of the lesion is always kept well in mind. The tear in the media from which the dissection originates is most commonly situated in the ascending

aorta, a little distal to the aortic valve. Next most common is a tear just distal to the left subclavian artery often associated with some degree of true aneurysmal dilatation of this part of the aorta. As the blood dissects downwards in the coats of the aorta the side vessels are affected in a variable manner. The dissection may extend outwards along these vessels; they may be enveloped and passed; they may be occluded; or they may be torn across at their origins. The dissection usually bursts through the outer coat of the aorta into the pericardium, mediastinum or pleura, but only rarely into the peritoneum or retroperitoneal tissues. Very rarely, the dissection re-enters the normal lumen of the aorta through another tear in the media lower down, and a spontaneous cure results. It is this natural re-entry tear which gives the clue to surgical treatment. In view of the rapidly progressive nature of the condition and its high mortality, I believe that all cases in a reasonable general state should be treated by urgent operation.

Warren *et al.* (1956) suggested that the aims of treatment should be: (1) The establishment of re-entry of the dissection into the normal lumen, (2) The prevention of distal extension of the dissection, (3) The relief of peripheral arterial obstruction, if present, (4) The control of hæmorrhage, if present.

In my opinion the approach to the aorta should be transthoracic, except when peripheral arterial obstruction is present or in the rare cases in which intra-abdominal hæmorrhage has occurred. The main method of treatment is to clamp the aorta in two places just below the left subclavian artery and divide it between the clamps. In the distal end the media is then approximated to the outer coat of the aorta by suturing. In the proximal end the media is cut back at one point to form a re-entry hole of adequate size and the remainder of the media is sutured to the outer coat (Fig. 1), after which the two ends of the aorta are re-sutured as an ordinary end-to-end anastomosis. Creech *et al.* (1956) point out that the re-entry hole in the media should be close to the origin of the dissection in order to minimize the risk of bursting of the outer coat of the dissection. The portion of the aorta just below the left subclavian artery is the highest point at which this can easily be done. If, on the other hand, distal vessels are occluded or intra-abdominal hæmorrhage is present, the aorta should be approached through the abdomen. A similar procedure is carried out to the dissecting aneurysm and normal blood flow through the occluded vessels re-established by the simplest means. Creech *et al.* (1956) state that in those cases in which the dissection starts below the left subclavian artery

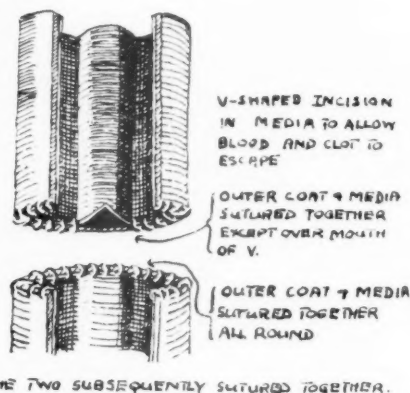


FIG. 1.—Normal method of repair.

and there is an associated true aneurysmal dilatation of the aorta, the affected portion of the aorta should be excised from above the tear in the media and replaced with a graft.

CASE HISTORY

A man aged 59 was admitted to the Norfolk and Norwich Hospital on the evening of November 4, 1956. About one month previously at an examination for insurance he had been found to have fairly severe symptomless hypertension. One hour before admission, he had suddenly developed a severe pain in the lower thoracic region of his back which radiated round both sides to the front at about the level of the costal margins. Soon after the pain started he felt "pins and needles" in his left leg followed by numbness of this leg. Examination showed that he was in great pain. His pulse was 68 per minute, regular, and could be felt in both arms. His blood pressure was 290/150 and was the same in both arms. The heart sounds were normal and no murmurs were heard. There was no abnormality found in his chest or abdomen. His left leg was considerably colder than his right leg, although there was no obvious change in colour. All pulses in the left leg were absent, but were normal in the right leg. A diagnosis of dissecting aneurysm of the aorta with occlusion of the left iliac artery was made. It was decided that urgent operation was indicated and in view of the occlusion of the left iliac artery it was decided that the aorta should be explored through the abdomen. In case it might prove necessary to clamp the aorta above the renal arteries, it was felt wise to perform the operation under hypothermia. The patient was therefore anaesthetized and hypothermia was induced by surface cooling. The abdomen was opened through a long left paramedian incision. There was no blood or fluid in the peritoneal cavity and the gastro-intestinal tract was normal. The aorta was exposed and a dark bluish discoloration was seen on its left side occupying about one-third of its circumference. The renal, mesenteric and right common iliac arteries were pulsating normally, but there was no pulsation to be felt in the left common iliac

artery. The bluish discoloration of the aorta was seen immediately below the diaphragm, and had obviously started above this. It extended down the full length of the left side of the abdominal aorta and then spread out to envelop the whole circumference of the left common and external iliac arteries (Fig. 2). To restore the circulation to the left leg,

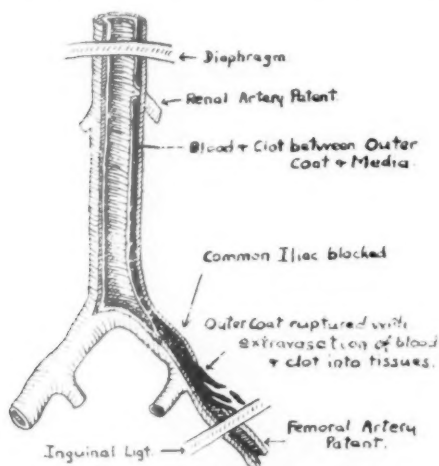


FIG. 2.—Diagram of findings at operation I.

a clamp was applied to the top of the left common iliac artery and the vessel was divided below. The proximal end of the vessel was found to be partially occluded by the dissection in its coats, but it was found possible to wash out and remove the blood and clot from within its coats so that the lumen was restored almost fully. The distal end of the vessel was completely occluded by the dissection in its coats, and it was found impossible to remove or wash out the blood and clot, so that its lumen could not be restored (Fig. 3). It was then decided to explore the left femoral artery to see if its lumen was occluded or not. The left femoral artery was therefore exposed just below the inguinal ligament. During the course of the dissection it was found that there was an extravasation of blood in the tissues around the artery, and it was therefore felt that the outer coat of the dissecting aneurysm had already begun to burst, probably somewhere just above the inguinal ligament. The left femoral artery itself appeared to be normal with a good lumen free of clot (Fig. 2). It was decided to restore the circulation to the left leg by means of an artery homograft, and at the same time to establish a re-entry hole through the media for the dissecting aneurysm.

The media and the outer coat of the proximal end of the left common iliac artery were approximated by a continuous arterial suture for about three-quarters of its circumference. At the remaining quarter of the circumference the media was cut back as an inverted V in order to form a re-entry hole (Fig. 4). The upper end of the graft was anastomosed end-to-end to the proximal part of the common iliac artery,

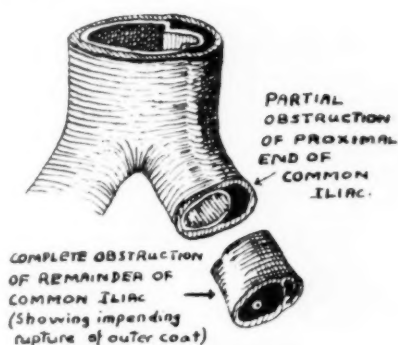


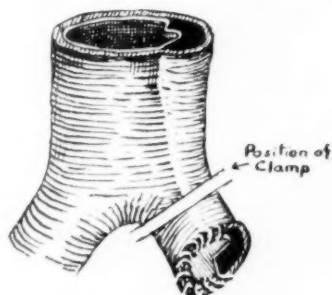
FIG. 3.—Findings at operation II.

sutured to all layers over three-quarters of the circumference and to the outer coat only over the part where the media had been cut to form the inverted V. The lower end of the graft was passed under the inguinal ligament and anastomosed end-to-side to the femoral artery.

On releasing the clamps, normal pulsation was restored throughout all the arteries of the left leg. It was realized that the re-entry hole through the media had been established a very long way below the original tear in the media, but the patient's general condition would not allow a further operation to be performed on his chest in order to establish a further re-entry hole there. It was therefore decided that nothing further should be done and the patient was returned to the ward.

He made an uneventful post-operative recovery except that on the fourth post-operative day his blood urea had risen to 80 mg. % but he passed a good volume of urine throughout. By the fourteenth post-operative day, the blood urea had fallen again to 38 mg. %. He was discharged on November 30, 1956, twenty-six days after admission.

While the patient was still in the hospital, my



V-Shaped incision in media.
Suture of media to outer coat except over mouth of V.
Subsequent anastomosis of this to graft.

FIG. 4.—Operative procedure.

colleague, Dr. J. A. Campbell, started treating him for his hypertension and the patient has remained under Dr. Campbell's care ever since. He has been treated with Serpasil and Inversine and on January 16, 1959, his blood pressure was 155/90. He was then very fit and well and took exercise every day by walking about one mile in spite of the snow which was present in Norwich at that time.

I should like to thank my colleague, Mr. A. P. Bentall, for all the trouble he has taken in preparing the diagrams.

REFERENCES

CREECH, O., DEBAKEY, M. E., and COOLEY, D. A. (1956) *Texas St. J. Med.*, **52**, 287.

GURIN, D., BULMER, J. W., and DERBY, R. (1935) *N. Y. St. J. Med.*, **35**, 1200.

LEVINSON, D. C., EDMAN, D. T., and GRIFFITH, G. C. (1950) *Circulation*, **1**, 360.

MARTIN, P., and MUIR, J. D. (1958) *Brit. med. J.*, **i**, 441.

SHENNAN, T. (1934) *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 193.

SWANN, W. K., and BRADSHAW, J. I. (1956) *New Engl. J. Med.*, **255**, 36.

WARREN, W. D., BECKWITH, J., and MULLER, W. H. (1956) *Ann. Surg.*, **144**, 530.

Mr. T. HOLMES SELLORS showed a film entitled **Atrial Septal Defect**. (See *Lancet*, 1957, **i**, 1255.)

Meeting

May 1-2, 1959

MEETING AT BRISTOL

Programme

May 1, morning, at the Royal Infirmary

The following operations were performed:

Femoropopliteal Artery Graft.—Mr. R. HORTON.

Thyroidectomy.—Mr. ROBERT COOKE.

Porta-caval Anastomosis.—Professor R. MILNES WALKER.

Operation for Vesico-colic Fistula.—Mr. ASHTON MILLER.

Scientific demonstrations and cases of surgical interest were on show during the morning, together with an X-ray quiz competition set up by Dr. J. H. MIDDLEMISS.

May 1, afternoon, at the Council House

The following papers were read and films shown:

The Treatment of Window Fistula.—Mr. D. G. J. JENKINS.

Cineradiography of the Common Bile and Pancreatic Ducts.—Dr. F. G. M. ROSS and Mr. P. J. W. MONKS.

Hazards of Surgical Diathermy.—Mr. J. P. MITCHELL.

Diagnosis of Colon Polyps.—Dr. J. H. MIDDLEMISS.

Carcinoma of the Duodenum.—Mr. K. D. J. VOWLES.

Film: Bilateral Oophorectomy and Adrenalectomy in a Single Stage.—Mr. D. S. M. BARLOW.

Neuromuscular Enteropathy.—Dr. J. M. NAISH and Mr. W. M. CAPPER.

May 2, morning, at Frenchay Hospital

The following operations were performed:

Plastic Department

Excision of Rodent Ulcer Involving Skull Bone of Temporal Region, and Scalp Flap.—Mr. G. FITZGIBBON.

Reconstruction of Mandible by Bone Graft Following Resection from Angle to Angle Two Years Ago for Carcinoma.—Mr. D. C. BODENHAM and Mr. W. BAKEWELL.

Film showing Forehead Flap Technique.—Mr. D. C. BODENHAM.

Neurosurgical Department

Subacute Subdural Haematoma.—Mr. G. L. ALEXANDER.

Torkildsen's Operation (Ventriculo-cisternal By-pass) for Pineal Tumour.—Mr. D. G. PHILLIPS.

Thoracic Department

Dismantling of Previous Gastro-enterostomy and Oesophagogastricomy for Benign Stricture of the Oesophagus.—Mr. R. H. R. BELSEY.

Repair of Hiatus Hernia.—Mr. D. MEARN MILNE.

General Surgery Department

Operation for Large Incisional Hernia.—Mr. C. H. BARTLETT.

The following papers were read:

Colon Transplant for Oesophageal Replacement.—Mr. R. H. R. BELSEY.

Pancreatic Function after Gastrectomy.—Mr. T. J. BUTLER.

The Radiological Department also showed a series of short films.

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Section of Proctology

President—HENRY R. THOMPSON,
M.A., M.B., F.R.C.S.

Meeting

January 14, 1959

(continued from *Proceedings*, May 1959, p. 390)

Non-specific Anal Ulceration

By C. PATRICK SAMES, M.S.

Bath

THESE remarks are based upon experiences from three problem cases which have come under my care in the last few years.

The first was a woman referred by a physician for sigmoidoscopy, because of severe diarrhoea of some months' standing, and suspected of ulcerative colitis. Sigmoidoscopy was normal to 30 cm., but proctoscopy revealed two shallow ulcers in the anal canal, together with a skin tag which was partly granulation tissue, and a shallow subcutaneous fistula-in-ano. The rather weak bluish unhealthy granulations, the undermined edges and the thin seropurulent discharge suggested tuberculosis. She also had peri-articular thickening of the joints of the hands and wrists, ulcers on the tongue and palate and a phlyctenular type of conjunctivitis.

With a tentative diagnosis of tuberculosis I removed the partly ulcerating skin tag, laid open the fistula and generally improved the drainage.

The biopsy report was non-specific granulation tissue with no evidence of tuberculosis. The E.S.R. was persistently raised to over 80 mm. in the 1st hour (Westergren) and the haemoglobin fluctuated around 45–55%. Barium enema and barium meal were both negative, and without any evidence of ulcerative colitis or Crohn's disease. Several searches were made for L.E. cells; Rose's test was always negative and serum Wassermann and Kahn reactions likewise.

The ulceration of the anal canal and perianal skin refused to heal despite every effort. Exposure to ultraviolet light and infra-red made no impression. Several searches were made for unusual anaerobic organisms, for amoebae, and even *Giardia lamblia*, all without results. Despite cortisone therapy, heavy doses of vitamins and even a course of mepacrine the condition, rather than improving, became gradually worse.

In an attempt to arrest its slow but relentless advance I resorted to diathermy excision, on the lines of treatment recommended for symbiotic synergistic gangrene. This was followed by an appreciable reactionary haemorrhage, which she could ill afford. The diathermy excision

proved no better than the other forms of treatment; and the ulceration advanced and began to involve the sphincter muscles. At this stage I resorted to a defunctioning left iliac colostomy; but despite this there was no dramatic response. After waiting six months, at the patient's own request, in fact entreaty, and with a disturbed conscience, I resorted to an abdominoperineal resection, leaving the patient with a permanent terminal colostomy with which she is more than satisfied. Her total stay in hospital was fifteen months and the duration of her illness two and a half years. I saw her recently and she is well, having put on weight, and with a sound perineal scar.

At the time I was dealing with this patient there appeared an account of Behcet's syndrome (Phillips and Scott, 1955, *Lancet*, i, 366). The ulceration in this condition is usually of the vulva, but there is in addition a rheumatoid type of arthritis and conjunctivitis very reminiscent of those just mentioned. The ulceration of the anal canal, being only a little removed from the vulva, prompts the suggestion that this condition may have been a variant of the syndrome, except for the fact that in Behcet's syndrome the ulcers are typically very painful, and there is a tendency to spontaneous healing, with relapses.

A similar case was referred to me from the Royal National Hospital for Rheumatic Diseases in Bath. This patient was suffering from spondylitis of the Marie-Strümpell type, and rheumatoid arthritis of the ankles and feet. In addition she had a persistent anal and perianal ulceration which on closer examination revealed a low proctovaginal fistula. Like the previous case she had a persistently high E.S.R. and secondary anaemia, but all other investigations, as in the former case, were unrewarding, including searches for L.E. cells, and Rose's test. The bowel was normal for 30 cm. above the lesion. The ulceration was curiously painless and troubled her very little; it had been present for several months. Having met with so little success in the previous case, I have as yet avoided

surgery except for examination under anaesthesia and repeated biopsies for histology.

The third case occurred in a mentally defective patient. All investigations have proved negative, except that biopsy showed some equivocal giant cell systems (but no tubercle bacilli). X-rays of the chest were negative and there is no evidence of other disease. On the strength of the few giant cell systems she was put on a three-months' course of streptomycin, PAS and isoniazid, but a recent inspection shows no improvement; in fact, the reverse, the sphincters now becoming eroded.

One other patient who may have some bearing on the aetiology of these cases was a man who had a one-stage total colectomy and ileo-rectal anastomosis for an acute exacerbation of a relapsing ulcerative colitis. The result is not good; the patient is unhappy. At his best he has 8 stools per day, at his worst, 12; there are 1-3 at night. He is a publican and insists on continuing his beer, and that may be a factor.

He has a considerable ano-proctitis and persistent ulceration of the median raphe of the perineum.

We have, I am sure, all seen cases of non-specific granular proctitis which have slowly spread upwards to give rise to ulcerative colitis. Likewise we have seen ulcers, similar to those I have described, in association with established ulcerative colitis. I wonder whether these ulcers, which occur alone, could be an anal and perianal manifestation of one and the same disease? Also are we correct, when rheumatoid arthritis complicates ulcerative colitis, in regarding it as cause and effect? Might there not be a common aetiological factor?

These ulcers which I have described are characterized by chronicity and a relentlessly progressive nature, are curiously painless and intransigent to treatment; and as far as I am aware are of unknown aetiology.

Mr. C. I. COOLING (London) read a paper entitled **Proctology and the Undergraduate**.

Meeting
February 11, 1959

The Management of the Perineal Wound After Abdomino-perineal Resection

Why Leave the Perineal Wound Open?

By DONALD BARLOW, M.S., F.R.C.S.

London

Introduction.—Those who have had the care of cases after abdominoperineal resection of the rectum cannot fail to be touched by the sufferings of patients who undergo repeated packings and dressings of a large perineal wound.

Primary closure of the perineum is a practical proposition in the majority of cases. Experience in both thoracic and general surgery allows the principles of the one to be applied with advantage to the other.

It has been customary in general surgery to believe that a large cavity left in the body after a major resection requires drainage. This is untrue provided haemostasis is complete and provided there is no mucus-secreting or actively discharging source of infection into the cavity. If serum accumulates, as it often does, it can be left alone unless it bulges the perineum unduly—when it can be aspirated.

In pneumonectomy, even where the lung has been full of pus and where it had already perforated and formed an empyema, the chest can be safely closed without drainage, again provided the bronchus is completely closed and covered with a living graft, haemostasis assured and any empyema excised.

Abdominoperineal resection.—Some years ago, these reflections led the writer to wonder whether after abdominoperineal resection, the perineal wound could not be closed with safety.

Owing to the difficulty in keeping a satisfactory perineal dressing in position, sepsis and even secondary haemorrhage were not infrequent. Urinary difficulties, the need for prolonged catheterization, and later urinary sepsis were matters of moment.

The writer first closed a perineal wound completely some six years ago. Earlier he had closed the perineum but used a closed drain with slight suction. This was soon abandoned, as it was in the case of pneumonectomy, because of risk of sepsis and because the drain was unnecessary.

After radical surgery the levatores ani have largely gone but there is plenty of fatty tissue and skin to bring together in a good thick wound closure.

Routine closure is now adopted except in rare cases where special contraindications apply. Average convalescence is two to two and a half weeks. If complete closure is more widely adopted, resection of the rectosigmoid will lose

its sinister reputation and patients will be able to go home in as short a time as they would after a simple laparotomy. As with complete closure after pneumonectomy, sterile fluid may persist for a while within the lower pelvis.

Urinary troubles are minimized and normal urinary flow is established after twenty-four to forty-eight hours.

Some essential details require attention:

(1) Haemostasis must be exact and painstaking. It is the writer's practice to avoid the synchronous combined method and instead to do the whole of the operation himself. A thorough clearance of the pelvic tissues is carried out including the removal of the greater part of the levatores ani, but the extent of the evacuation of the pelvic floor depends to some extent on the site of the growth. The peritoneum is not closed until, by inspection with powerful beamed lights, the surgeon is satisfied that the field is dry, but however dry the field is, the cavity none the less does tend to fill later with serum and blood. The essential point is to prevent this becoming

infected. Thus a strictly aseptic technique must be used throughout the operation and a long time should be spent in thoroughly sterilizing the whole of the perineal skin.

(2) An end colostomy is established. It is a mistake to use a "loop" type of colostomy if a preliminary colostomy is required. If it is necessary, two separate ends should be made—the proximal through a stab trans-rectal incision so that it can later be excised at the major operation, i.e. there must be no question of a distal colostomy stump in the wound. Complete closure is impracticable if a perineal, as opposed to abdominoperineal, resection is performed.

(3) If, in the course of operation, it proves necessary to do a hysterectomy because of malignant involvement of the uterus, total removal of the latter is required and the roof of the vagina properly invaginated. If the cervix remains, this leaves a potentially secreting surface. Similarly, in the male, if the seminal vesicles are damaged, primary complete closure is inadvisable. Catgut only is used for ligatures.

CASES

Lymphosarcomatous Polyposis of Small and Large Intestine with Diverticular Stricture of Pelvic Colon.—T. D. McLARTY, M.D., F.R.C.S. (for HENRY R. THOMPSON, F.R.C.S.).

A male 75 years of age presented with a two-month history of 6–10 loose stools a day. No rectal bleeding. His only other complaint was vague abdominal discomfort without localization. Weight loss of 1 st. in the past year. Past and family histories not significant.

On examination.—Slight abdominal distension without tenderness. On rectal examination a diffuse nodularity was apparent on palpation, and on sigmoidoscopy numerous pale polypoid lesions were observed.

Laboratory and blood examinations were normal.

A barium enema showed a stricture in the pelvic colon and numerous polyps throughout the large bowel.

Laparotomy (H.R.T.) was carried out because it was felt the symptoms were semi-obstructive due to the stricture in the pelvic colon. At operation polypoid lesions were present in the gastro-intestinal tract from the duodenum to the anus. In the distal large bowel, the mucosa was almost obscured by polyps. The spleen and liver were enlarged and there were large soft mesenteric and para-aortic lymph nodes.

A Hartmann's operation with mid-transverse colostomy and resection of distal colon was carried out. In the resected specimen, as well as large numbers of smooth round polyps, there

was an area of diverticulitis 3 in. (7.5 cm.) long in the sigmoid colon, with narrowing of the lumen, fibrosis and abscess formation in the pericolic fat.

Histology.—The polyps were composed of a mass of lymphocytes covered by attenuated mucosa. There was invasion of the submucosa at a number of sites. The appearance was that of a diffuse lymphosarcoma of the colon, the polyps being the result of neoplastic proliferation of the intestinal lymph follicles. The pericolic and aortic nodes showed loss of differentiation. In the region of diverticulitis there was neoplastic proliferation within the diverticula.

Six months post-operatively, the patient is active and carrying on his normal activities.

Perforated Meckel's Diverticulum from Peptic Ulceration with Simultaneous Haemorrhage.—P. E. B. HOLMES, F.R.C.S. (for HAROLD EDWARDS, C.B.E., M.S., F.R.C.S.).

A male child, 10 months old, who had been treated for anaemia and abdominal pain on several occasions, was brought to hospital with severe intestinal colic associated with vomiting. Laparotomy revealed a large quantity of free dark blood in the peritoneal cavity, the cause being a perforated peptic ulcer at the base of a Meckel's diverticulum, lined by gastric epithelium. Resection of the gut bearing the diverticulum was performed with uneventful recovery.

The occurrence of haemorrhage with perforation is a combination rarely reported. The age of the child is also unusual.

Regional Colitis.—IAN P. TODD, M.S.

Mr. L. K., aged 52, presented with a clinical history of incomplete large bowel obstruction of three weeks' duration, commencing after a large rectal hæmorrhage. A similar bleeding episode occurred five years previously, but between these bowel function had been normal.

An episode of bacillary dysentery occurred while he was on military service in Algiers twenty years previously.

Physical examination, which included sigmoidoscopy to 17 cm., revealed no abnormality.

Investigations.—Hæmoglobin 94%. W.R. and Kahn negative. Barium enema: An irregular stricture 8 in. (20 cm.) long was visible in the region of the splenic flexure; the remainder of the colon appeared normal (Fig. 1).



FIG. 1.

Operation.—The abnormal area of colon was resected and bowel continuity restored. There was no disease evident in the remainder of the colon, or in the small bowel. The other abdominal viscera were normal. Post-operative recovery was uneventful.

Pathology report.—"Appearances: There is an area of shallow ulceration about 7 in. (17.5 cm.) in length and 2 in. (5 cm.) wide which is confined to the mesenteric half of the bowel wall. The anti-mesenteric half of the intestine is distended and sacculated but its mucous membrane appears normal. The regional lymphatic glands are slightly enlarged."

Histology.—"Sections show non-specific chronic inflammatory ulceration of the mucous membrane with œdema and fibrosis of the

submucosa. The underlying muscle is thickened and corrugated but is otherwise normal. The regional lymphatic glands show a non-specific hyperplasia only. The inflammatory cell reaction is slight and there is evidence of healing."

He has remained well since the operation, with no disturbance of bowel function; to date, however, this is only a period of ten months.

Multiple Carcinomata of Colon in a Case of Chronic Ulcerative Colitis with Hepatic Cirrhosis.—L. R. DE JODE, F.R.C.S. (for E. C. B. BUTLER, F.R.C.S.).

A. T., female, aged 32. Housewife.

History.—1942: Jaundice lasting six weeks. 1945: Onset of diarrhoea with blood and mucus in stools; during the subsequent five years had several attacks with periods of remission. 1949: Spleen enlarged 3 fingerbreadths below left costal margin. Sigmoidoscopy showed congested rectal mucosa, which bled easily, but no ulceration was seen. **Investigations** at this time: Hæmoglobin 80%. Thymol turbidity 13.1 units. Albumin/globulin = 3.8/3 grams %.

1950: Staphylococcal right perinephric abscess drained. 1953: Normal pregnancy; patient remained well during this time. 1954: Further exacerbation; passing blood and mucus in stools up to five times a day. Hæmoglobin 56%. Following blood transfusion, she improved and from this time until her last admission was remarkably well, passing between 1 and 3 formed stools daily.

15.12.58: Sudden onset of central abdominal pain, later shifting to right iliac fossa.

18.12.58: Laparotomy for acute appendicitis disclosed multiple carcinomata of colon, and obstructive appendicitis secondary to a carcinoma of the cæcum. Appendicectomy (Harold Wood Hospital).

23.12.58: Transferred to London Hospital.

On examination.—Slight fever, recent wasting, pallor and finger clubbing. Spleen enlarged.

Investigations.—Barium enema showed a rigid colon with loss of haustration, and areas of narrowing in the mid-transverse colon and just proximal to the splenic flexure. No active ulceration. Sigmoidoscopy demonstrated a red, œdematous mucosa, but no ulceration seen. Thymol turbidity 3 units. Albumin/globulin = 3.5/3.4 grams %. Hæmoglobin 76%.

Subtotal colectomy and ileo-rectal anastomosis (6.1.59).—Findings: Quiescent ulcerative colitis with an obvious carcinoma of the cæcum, and three indurated strictures, in the transverse colon, splenic flexure and pelvic colon respectively. A number of small glands in the mesentery were present. The liver was shrunken and cirrhotic. In view of the known poor prognosis in these

cases, an immediate ileo-rectal anastomosis was carried out.

Post-operative progress.—On the fifth post-operative day sudden collapse occurred. Re-operation showed peritonitis due to an anastomotic leak, and ileostomy was performed. However, the patient developed progressive hepatic failure with increasing jaundice and died eleven days later.

Post-mortem examination showed two hepatic metastases in a cirrhotic liver.

Specimen showed diffuse colitis with, however, minimal ulceration—the “cobblestone” appearance. The ileum was healthy. There was a proliferative nodular carcinoma of the caecum. There were three malignant strictures: in the right half of the transverse colon, just proximal to the splenic flexure, and in the pelvic colon.

Histology.—Diffuse colitis with localized ulcerations; the submucosa fibrosed and lightly infiltrated with round cells. The microscopic appearance of the four carcinomata supported the view that they were independent primary growths.

Comment.—The long history preceding the development of carcinoma when this occurs in ulcerative colitis is well recognized, but of particular interest here is the quiescence of the disease, a feature noted in some cases by Dukes and Lockhart-Mummery (1957).

Diagnosis is often difficult, and only the development of one of the carcinomata in the caecum resulting in obstructive appendicitis led to a diagnosis at laparotomy. The clinical diagnosis is easily overlooked because the symptoms of carcinoma are ascribed to an exacerbation of colitis, and, moreover, opaque enema studies may be inconclusive, showing, as in this case, only some segmental narrowing, which may occur in benign strictures. Indeed, as pointed out by Counsell and Dukes (1952), these carcinomata may often present as localized strictures, and both the macroscopic and microscopic appearances may be atypical.

Acknowledgments.—This patient was under the medical care of Professor Clifford Wilson, by whose courtesy the case is shown. Acknowledgment is made to Professor Dorothy Russell, for the pathological findings.

REFERENCES

- COUNSELL, P. B., and DUKES, C. E. (1952) *Brit. J. Surg.*, **39**, 485.
 DUKES, C. E., and LOCKHART-MUMMERY, H. E. (1957) *Brit. J. Surg.*, **45**, 25.

Colo-uterine Fistula Due to Diverticulitis of Pelvic Colon.

—PAUL T. SAVAGE, F.R.C.S.

Miss E. C., aged 73.

History.—In May 1956 she first complained of left-sided lower abdominal pain and diarrhoea, with a little blood in her motions.

Examination showed a mobile swelling 2 in. (5 cm.) in diameter in the pouch of Douglas. Sigmoidoscopy to 25 cm. showed nothing abnormal. Barium enema: Extensive diverticulitis of pelvic colon.

At operation.—Extensive diverticulitis of pelvic colon was noted, and a Brenner tumour of the left ovary removed. Following this she remained well until October 1958 when she complained of a blood-stained vaginal discharge, which later became faeculent.

Physical examination and investigations.—Wizened, kyphotic, healthy old lady of 73. Blood pressure 170/100. Vaginal examination showed a faeculent discharge coming from the cervix. Dilatation and curettage showed purulent endometritis only; no evidence of carcinoma. Hystrogram showed that the contrast medium passed from the body of the uterus into the pelvic colon and rectum. Barium enema again showed extensive diverticulitis of pelvic colon, but the fistula could not be outlined (Fig. 1).

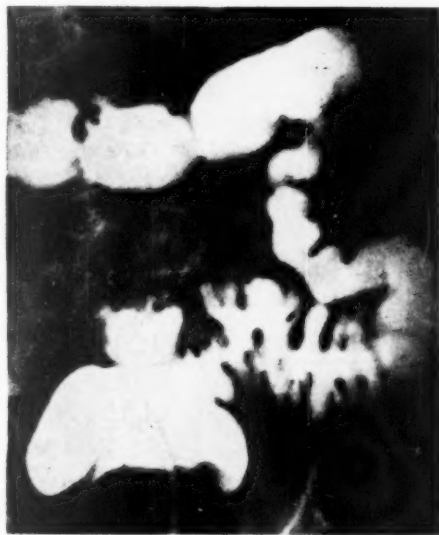


FIG. 1.—Barium enema showing extensive diverticulitis.

Operation.—The pelvic colon and rectosigmoid showed extensive diverticulitis. The pelvic colon was found to be adherent to the left cornu of the uterus. The only other abnormality was very extensive jejunal diverticulosis.

A combined total hysterectomy and left hemicolectomy was carried out. Continuity of the bowel was restored by anastomosing the splenic flexure to the upper third of the rectum.

Convalescence was uneventful.

Perforated Diverticulum of Sigmoid Colon and Carcinoma of the Rectum.—FRANK FORTY, F.R.C.S.

W. S., male, aged 51, was admitted to Edgware General Hospital on 24.7.58.

History.—Abdominal pain, mainly in left iliac fossa, for four days, sudden onset. Occasional bleeding *per rectum* during past few days. Increasing constipation for one year.

On examination.—Tenderness and guarding in left iliac fossa. Abdomen not distended. Normal bowel sounds. *Per rectum:* Carcinoma felt high in the rectum.

First operation.—Findings: Inflammatory swelling of sigmoid colon stuck down to pelvic floor and surrounded by local abscess containing pus; the appearances were those of diverticulitis. Procedure: Drainage of abscess; transverse colectomy. Healed uneventfully.

Second operation.—Abdominoperineal excision of the rectum. All signs of previous inflammation of the sigmoid had disappeared. No secondaries

in liver or other remote metastases. Uneventful recovery.

Specimen.—A small carcinoma just below the rectosigmoid junction; a perforated diverticulum was evident about 1½ in. (4 cm.) above the growth, and presumably had been only lightly sealed by lymph; marked absence of surrounding inflammatory reaction.

Table I shows the operations performed in a series of 23 cases of perforated diverticulitis.

TABLE I.—PERFORATED DIVERTICULITIS. 23 CASES

| | |
|-----------------------------------|---|
| OPERATION: Resection and drainage | 7 |
| Colostomy and drainage | 9 |
| Colostomy alone | 1 |
| Drainage alone | 1 |
| Perforation oversewn | 2 |
| Exteriorization | 2 |
| Exploratory laparotomy | 1 |

3 deaths occurred in the series; 2 following resection and drainage and 1 after exteriorization. Causes of death were small intestinal obstruction on 2 occasions and a residual pelvic abscess in 1.

Meeting

March 18, 1959

MEETING HELD AT ST. MARK'S HOSPITAL, LONDON

The following papers were read:

Inflammatory Diseases of the Colon other than Ulcerative Colitis.—Dr. B. C. MORSON and Mr. H. E. LOCKHART-MUMMERY.

Cancer Control in Polyposis Families.—Dr. C. E. DUKES (*see Dis. Colon Rectum*, 1958, 1, 413).

Demonstrations were given and cases were shown and the following operations carried out:

Submucous Hæmorrhoidectomy (two cases).—Mr. A. G. PARKS.

Sphincterotomy for Fissure-in-ano (two cases).—Mr. A. B. VIVIAN.

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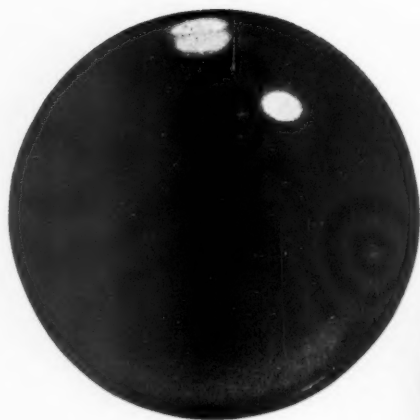
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¹ Rosa, L., et al., *Acta allerg.* (Kbh.), 1957, **XI**, 81



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Section of Epidemiology and Preventive Medicine

President—Sir JAMES KILPATRICK, K.B.E., C.B.

Meeting
March 20, 1959

Q Fever: Recent Developments and Some Unsolved Problems [Abridged]

By B. P. MARMION, M.D.

Leeds

A GREAT deal has been written about Q fever and the mass of literature which has accumulated might easily give the impression that the problem was completely worked out. However, although the main facts about the clinical aspects of the disease and the ecology of the rickettsia are now fairly clear and familiar, some problems still remain. In an effort to justify this statement I shall discuss recent findings and unsolved problems in relation to three arbitrarily selected and unrelated aspects of Q fever.

Pathogenesis of the disease.—Q fever in a human being is well known as a short-lived febrile illness and after the encounter host and parasite appear to go their separate ways. However, other rickettsiae have been shown to persist in the host for variable periods after an initial infection, the most striking example being that of Brill's disease. It now seems that *R. burneti* may also persist in various hosts, either as a latent or an overt and chronic infection.

Perhaps the best demonstration of a latent and recrudescent infection with *R. burneti* is to be found in the pregnant animal—human being, domestic ruminant or laboratory experimental animal. It has been shown by American workers (Abinanti *et al.*, 1953; Parker *et al.*, 1949) that sheep and cattle inoculated experimentally with *R. burneti* in the early stages of pregnancy undergo a mild apparent or inapparent infection with the rickettsia which then remains latent until parturition when it is found in large numbers in the products of conception, and also in urine and faeces. This phenomenon has an added interest in view of the recent observations by Syrucek *et al.* (1958) who isolated *R. burneti* from human placentas collected at births occurring two to three years after an original Q fever infection.

Abinanti, in some work carried out at Cambridge, found that *R. burneti* could be recovered in fairly large numbers from the placentas or fetuses of guinea-pigs inoculated with small doses of the rickettsia, either in the

early stages of pregnancy or at varying periods up to 92 days before conception. Further, the organism could be recovered from the guinea-pig placenta early in pregnancy and in large numbers just before parturition, but was not detected in the mid-period (Abinanti, 1957).

The results with the guinea-pigs were somewhat similar to those previously obtained in sheep by the North Californian workers (see Abinanti, 1957) who found that *R. burneti* could be recovered from various organs of pregnant ewes for a few weeks after experimental inoculation but that it could not be isolated from the placenta until just before or at parturition. Abinanti also found that the recrudescent infection at parturition occurred in guinea-pigs with high levels of antibody—including that to the Phase I complement-fixing antigen of the rickettsia which we believe to be responsible for "neutralising" the organism *in vivo* (Abinanti and Marmion, 1957).

The apparent absence of the rickettsia from the placenta during the later stages of pregnancy in guinea-pigs and sheep, and its appearance at or just before parturition, poses an interesting problem. Has the rickettsia been in the placenta throughout pregnancy or has it found its way there late in pregnancy via the blood stream, starting from some other focus in the body? It is conceivable, though unproven, that the placenta is seeded early in pregnancy, perhaps even via the ovum, but that its physiological state does not permit extensive multiplication of the rickettsiae until near parturition.

Clearly the physiological reason for the late multiplication of the rickettsiae in the placenta is one of the unsolved problems of the disease and the investigation of this reproducible phenomenon might provide useful analogies for the understanding of recrudescent infection in other rickettsial diseases.

These speculations naturally bring to mind the possibility that a condition analogous to Brill's disease may occur in human Q fever.

At present there is no evidence that *R. burneti* can remain latent in human beings for as long as ten or fifteen years after an initial apparent or inapparent infection and then relapse, but as the disease is endemic in most areas of the world the difficulties of detecting such (hypothetical) cases are obvious. Nevertheless, quite apart from the women described by Syrucek *et al.* (1958), there is some evidence of the persistence of *R. burneti* in human beings for a substantial period. Drs. Robson, Shimmin and Andrews and I have recently investigated one such patient under the care of Dr. F. H. Scadding at the Middlesex Hospital. This man had an illness which was clinically typical of Q fever, recovered and was well for six months and then relapsed with a chronic febrile illness which lasted some eighteen months (Robson and Shimmin, 1959; Andrews and Marmion, 1959). *R. burneti* was recovered from his blood stream on two occasions during life and from various tissues after death. The patient had signs of aortic valve incompetence during his chronic illness and at autopsy a grossly distorted valve with small vegetations was found—the latter contained large numbers of *R. burneti* when titrated in guinea-pigs.

The clinical picture resembled that of subacute bacterial endocarditis with the important differences that *Strep. viridans* or other organisms were not isolated on repeated culture of the blood during life, and embolic phenomena were not a striking feature of the disease. This case, and a few less well-substantiated ones which have occurred in the past, raises the question of the importance of chronic Q fever infection as a cause of subacute endocarditis and that of the frequency of its misdiagnosis as subacute "bacterial" endocarditis. The response of most cases of subacute "bacterial" endocarditis to penicillin suggests that the problem is not a large one although the success with which viridans streptococci or other bacteria have been isolated from various series of patients with the clinical diagnosis of subacute bacterial endocarditis has varied considerably (see summary by Wright, 1925, and, more recently, Cates and Christie, 1951). Wright concluded that the failures were not due to inadequate technique and that bacteria were genuinely absent in his "non-septicemic" cases. He also examined the heart valve vegetations from 14 cases of subacute endocarditis whose blood had been sterile during life and, apart from some superficial contaminants in 3 cases, could see no definite bacteria in Gram-stained preparations. In 12 cases, however, there was some particulate material, smaller than cocci, which stained red with Twort's method. We are trying, therefore, to

reinvestigate the problem of the aetiology of those cases of subacute endocarditis with sterile blood cultures, bearing in mind the possibility of Q fever or other rickettsial infections.

The biological significance of infection in small animals and birds.—The early investigations of Derrick (1944) showed infection in bandicoots and two local species of rat, but these observations were soon overshadowed by the realization of the prime importance of domestic ruminants as hosts for the maintenance of *R. burneti*. In recent years, however, Italian workers (Babudieri and Moscovici, 1952) brought the problem forward again when they showed that pigeons and geese may be naturally infected. Czechoslovakian workers (Syrucek and Raska, 1956) have found serological or cultural evidence of Q fever in domestic hens, pigeons, turkeys, ducks, geese and also in various species of wild birds. Other investigations in the same country revealed infection in *Rattus norvegicus*, *Mus musculus*, other small rodents, and *Sorex minutus* (shrew mouse), (Raska and Syrucek, 1956; Raska *et al.*, 1956). It may also be recalled that infection has been found in mountain rabbits and dormice in Spain (Gallardo *et al.*, 1952) and in rabbits and ticks in Casablanca (Blanc and Bruneau, 1956).

The problem is essentially this: do these animals and birds represent a number of independent host systems in which *R. burneti* perpetuates itself indefinitely or, on the other hand, are they merely infected irregularly by contact with infected cattle and sheep and are they in fact incapable of perpetuating the rickettsia in series? Although this question is unsettled I suspect that, in the main, the presence of the rickettsia in these creatures represents merely a "spill-over" of infection from the main system of maintenance, domestic ruminants. Thus it is probably significant that examination of sera from hens in south-eastern England revealed infection among birds in close contact with sheep and cattle but not among those in an area with a few of these animals (see Marmion and Stoker, 1958). However, although it may be possible to dismiss infection in most small animals and birds as originating from that in domestic ruminants and of little biological importance, I doubt very much whether, for example, Derrick's observations on the apparently successful maintenance of infection in bandicoots and their ticks on the isolated Moreton Island off the Queensland coast can be so lightly discounted. The Czechoslovakian experience is particularly relevant and Dr. Syrucek will comment in detail on the significance of the excretion of *R. burneti* by experimentally-infected chickens and rats (Sobeslavsky, 1957; Syrucek

and Sobeslavsky, 1956) and on the biological importance of infection in creatures other than cattle and sheep.

The immediate sources of infection in outbreaks of Q fever in this country.—Since 1949 eleven outbreaks of the disease have come to light and investigations have been inconclusive for the most part. I am much indebted to Dr. W. W. Holland and his colleagues (Holland *et al.*, 1959) for some unpublished information about two outbreaks of Q fever in the R.A.F. in 1958 and also to Drs. G. J. G. King and J. C. Walker for information about cases in Dorset and Kent. On examining the features of ten outbreaks (excluding that in South Wales investigated by Baird and Evans, *see* p. 616) the following facts emerge. With one exception they all occurred in adults and predominantly among men. Children were only involved once—in a household outbreak on a farm—the youngest to show symptoms being 8 years old (Stoker and Thompson, 1953).

With Derrick's original observations in mind, it might be thought that outbreaks would be found almost entirely among people closely exposed to animals or animal products. In fact, although one outbreak in England did occur on a farm and another involved Welsh sheep farmers, the remainder occurred in such unlikely groups of the population as students at the Canterbury College of Art (Harvey *et al.*, 1951), men in an open prison, R.A.F. personnel, hospital staff and the actors in a religious play at a village in the Romney Marsh. The reason for these unusual settings is, I suspect, partly because of the lack of previous exposure, and therefore of immunity, in the groups concerned. The investigation of the play outbreak and the sporadic cases of Q fever in the Romney Marsh revealed that newcomers to the area, or new recruits to sheep farming, were those most often affected with Q fever. Presumably the long-term residents and the farming community were already well salted—either by exposure to infected milk, or in other ways (Marmion and Stoker, 1956).

The seasonal prevalence of the outbreaks is interesting. When those outbreaks originating from human sources are excluded it will be seen that the remainder occurred either in the spring or in the autumn (Fig. 1). Sporadic cases of Q fever also show an increase in numbers at these seasons and so we might conclude that the underlying factors directly or indirectly responsible for both sporadic cases and outbreaks are the same. Although these factors are probably complex there are some obvious correlations. Early in the year there is the spring calving, the lambing, and the shearing, and later in the year, the autumn calving (the

timing and pattern of these events varies, of course, from area to area). Any of these events might be the starting point of a short or long chain of infection which ends in an outbreak. However, like all correlations in time, these may be fallacious, and as a reminder of this I have also indicated in Fig. 1 the two seasonal prevalences (in Wales) of adult females of *Ixodes ricinus* which, in other countries, has been shown to carry *R. burneti*.

A consideration of the grouping of cases in time suggests that in eight outbreaks infection resulted from a single and short exposure to one (usually unidentified) source of infection. In two other outbreaks the temporal distribution of cases and other evidence suggests either infection from a number of distinct sources becoming infectious about the same time—probably different flocks of sheep which started to lamb at about the same time—or, less probably, infection from one unidentified source of persistent infectivity.

Infected milk does not seem to have been responsible for any of the outbreaks. In the outbreaks at the Cancer Hospital (Marmion and Stoker, 1950) and among the sick bay staff of a Cornish R.A.F. Station (Holland *et al.*, 1959) a human being with Q fever seems to have been the immediate source of infection. In three other outbreaks exposure to sheep, or to places contaminated by them, may have been responsible. As in other situations where the mode of transmission of infection is obscure the idea of air-borne infection has been invoked. Some recent air-sampling experiments by Welsh *et al.* (1958) demonstrate the distance to which

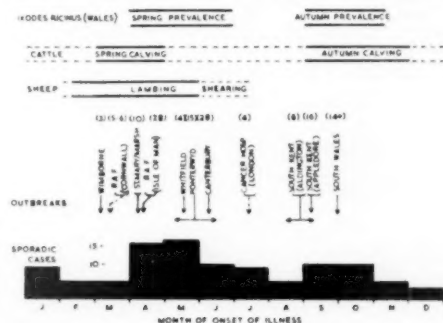


FIG. 1.—Seasonal distribution of sporadic cases and outbreaks of Q fever in England and Wales. Those outbreaks in which the cases occurred over a prolonged period are shown with horizontal lines and those originating from human sources are shown with dotted lines. The figures in brackets represent the number of people affected in the outbreaks. The commoner times of lambing, of spring and autumn calving, and the seasonal prevalences of *Ixodes ricinus* in Wales are also shown.

Rickettsia burneti can be disseminated through the air at the birth of a lamb from an infected ewe and the risk for bystanders is obvious. In addition, with an organism as hardy as *R. burneti*, when lambing takes place in a barn or in some other enclosed space, later visitors to the place might easily be infected from a persistent contamination of dust. However, this does not help much with outbreaks such as that at the Canterbury College of Art because no domestic animals had been on the premises. So we have to be a little more ingenious in devising chains of infection leading from the parturient animal to such environments. There are two main possibilities. The rickettsia might be carried from the scene of parturition in dust on various fomites—wool, hides, farm workers' clothing, &c., and subsequently be released as a secondary aerosol. Thus, cases of Q fever have occurred in wool sorters and we have isolated the organism from the clothing of a shepherd (Marmion and Stoker, 1956). Alternatively, the gap might be bridged by the secondary infection of small animals, birds or arthropods which, in turn, then excrete the organism in the vicinity of man. Thus, for example, hens might peck at infected sheep placentas and later excrete the organism in their droppings and so contaminate hen houses or the places where they are plucked and dressed for the table. Similar chains of infection involving rats and mice can be imagined.

Future investigators of unexplained outbreaks of Q fever in this country might pay more attention to the possibilities of carriage of the rickettsia by such animate, intermediate links in the chain of infection. Indeed various combinations of the animate and inanimate modes of carriage of *R. burneti* would seem to offer almost limitless possibilities to baffle the epidemiologist.

REFERENCES

- ABINANTI, F. R. (1957) Ph.D. Thesis, Cambridge.
 —, and MARMION, B. P. (1957) *Amer. J. Hyg.*, **66**, 173.
 —, WELSH, H. H., LENNETTE, E. H., and BRUNETTI, O. (1953) *Amer. J. Hyg.*, **57**, 170.
 ANDREWS, P. S., and MARMION, B. P. (1959) *Brit. med. J.* (in press).
 BABUDIERI, B., and MOSCOVICI, C. (1952) *Nature, Lond.*, **169**, 195.
 BLANC, G., and BRUNEAU, J. (1956) *Arch. Inst. Pasteur Maroc.*, **5**, 87.
 CATES, J. E., and CHRISTIE, R. V. (1951) *Quart. J. Med.*, **20**, 93.
 DERRICK, E. H. (1944) *J. Hyg., Camb.*, **43**, 357.
 GALLARDO, P. F., CLAVERO, G., and HERNANDEZ, S. (1952) *Rev. Sanid. Hig. públ. Madr.*, **26**, 81.
 HARVEY, M. S., FORBES, G. B., and MARMION, B. P. (1951) *Lancet*, ii, 1152.
 HOLLAND, W. W., ALLEN, B., FRENCH-CONSTANT, M., SMELT, C. M. G., TAYLOR, C. E. D., and ROWSON, K. (1959) To be published.
 MARMION, B. P., and STOKER, M. G. P. (1950) *Lancet*, ii, 611.
 —, — (1956) *J. Hyg., Camb.*, **54**, 547.
 —, — (1958) *Brit. med. J.*, ii, 809.
 PARKER, R. R., BELL, E. J., and STOENNER, H. G. (1949) *J. Amer. vet. med. Ass.*, **114**, 55, 124.
 RASKA, K., and SYRUCZEK, L. (1956) *Zent. f. Bact. (O)*, **167**, 267.
 —, —, SOBELAVSKY, O., POKORNY, J., PRIVORA, M., HAVLIK, O., LIM, D., and ZASTERA, M. (1956) *Csl. Epidem. Mikrobiol., Immunol.*, **5**, 246. Abstracted in *Trop. Dis. Bull.* (1957) **54**, 280.
 ROBSON, A., and SHIMMIN, C. G. D. L. (1959) *Brit. med. J.* (in press).
 SOBELAVSKY, O. (1957) *Csl. Epidem., Mikrobiol., Immunol.*, **6**, 146.
 STOKER, M. G. P., and THOMPSON, J. F. (1953) *Lancet*, i, 137.
 SYRUCZEK, L., and RASKA, K. (1956) *Bull. Wld Hlth Org.*, **15**, 329.
 —, and SOBELAVSKY, O. (1956) *Csl. Epidem., Mikrobiol., Immunol.*, **5**, 251.
 —, —, and GUTVIRTH, I. (1958) *J. Hyg. Epidem. Microbiol. Immunol.*, **2**, 29.
 WELSH, H. H., LENNETTE, E. H., ABINANTI, F. R., and WINN, J. F. (1958) *Ann. N.Y. Acad. Sci.*, **70**, 528.
 WRIGHT, H. D. (1925) *J. Path. Bact.*, **28**, 541.

An Interim Account of an Autumnal Outbreak of Q Fever in Cardiff

By A. D. EVANS, M.B., Dip. Bact., and T. T. BAIRD, M.B., D.P.H.

Cardiff

IN the years following its discovery by Derrick in 1937 and the isolation of *Rickettsia burneti* by Burnet (Burnet and Freeman, 1937), the world has had ample proof that "Q" for Query fever was well named. Derrick himself wrote that it was full of paradoxes.

The disease remained confined to Australia mainly as a hazard of meat workers until 1946, although Davis and Cox (1938) isolated an identical organism in Montana. Outbreaks were recognized in Greece (Caminopetros, 1948) and

Italy (Robbins *et al.*, 1946) in troops. Post-war, the disease can be found in most countries with a few notable exceptions—the Netherlands, New Zealand, Poland and Scandinavia (Kaplan and Bertagna, 1955). Nor has it yet been found in Ireland (Murdoch, 1959). In England Stoker found serological evidence of infection in 1949; shortly afterwards the first outbreak was reported (Harman, 1949; MacCallum *et al.*, 1949). Since then 7 outbreaks have been recorded (Marmion and Stoker, 1958).

Derrick found evidence of infection in bandicoots and isolated the rickettsia from their ticks. The role of the tick is still far from clear. He suggested (1944) that human infection might be due to inhalation of dried tick excreta from hides. More recent work in Greece and Italy (already quoted) and in California (Clark *et al.*, 1951; Huebner and Bell, 1951) has shown that a large reservoir exists in domestic ruminants. Slavin (1952) isolated *Rickettsia burneti* from 2% of pooled milk samples in Wales, and Evans (1956) found similar evidence of Q fever in 4.4% of herds near Cardiff. It has been shown that where the disease is endemic many wild and domestic animals and birds become infected (Babudieri, 1953; Syrucek and Raska, 1956).

The mode of transmission of the organisms is still obscure. Serological studies in Los Angeles (Bell *et al.*, 1950) indicated that infection was higher in cattle handlers and those who drank raw milk or lived close to stockyards. Rickettsia were shown (Welsh *et al.*, 1958) to be present in large numbers in the placenta, birth fluids and faeces. Many cases of Q fever in California could be explained by the inhalation of primary or secondary aerosols from these materials. These aerosols could cause cases far removed in time or space from the original source. In England and Wales several outbreaks could be explained on this basis including those at Aberystwyth (Report to Public Health Laboratory Service, 1956), Canterbury (Harvey *et al.*,

1951) and the one affecting actors in South Kent (Marmion and Stoker, 1956).

The pattern, however, varies in different countries. Marmion and Stoker (1958) concluded that man is usually infected from cattle and sometimes from sheep. They found that the chief method of spread appeared to be by milk, at least in the sporadic cases, but that some people had been infected at the birth of a calf and that proximity of residence to animals was probably not as important in this country due to our damper and less dusty atmosphere and the generally lower incidence of Q fever.

In spite of all this, our information about the epidemiology of Q fever is still limited.

The Cardiff Outbreak

Most outbreaks of Q fever have been diagnosed in retrospect (Derrick, 1953). We, on the other hand, have been fortunate in being able to start investigations while the patients were in hospital.

From Table I it will be seen that the ages of the patients ranged from 26 to 65 and that only 2 were female. This preponderance of adult males has been seen in several outbreaks (Marmion *et al.*, 1953), suggesting that there was an occupational origin. However, the occupations and the habits of the patients in this outbreak were essentially urban and no contact could be established between them.

The times of onset were between September 25 and October 10, 1958, in 13 of the cases whereas those of the others were spread over the next

TABLE I.—SHOWING AGE AND SEX DISTRIBUTION OF CASES, THEIR DATES OF ONSET, OCCUPATIONS, MILK SUPPLY AND CONTACTS

| Case no. | Age | Sex | Occupation | Onset | Q fever C.F. titre | Milk supply | Evidence of recent Q fever in family contacts |
|----------|-----|-----|----------------------|----------|--------------------|---------------|---|
| 1 | 52 | M | Steelworks inspector | 25.9.58 | 1/256 | Raw | 0/3 |
| 2 | 32 | M | Accountant | 26.9.58 | 1/8-1/128 | Dairy A Past. | 0/2 |
| 3 | 28 | M | Travelling salesman | 26.9.58 | 1/8-1/256 | Dairy A Past. | 0/1 |
| 4 | 45 | M | Truck driver | 27.9.58 | 1/128-1/512 | Dairy F Past. | 0/3 |
| 5 | 52 | M | Credit salesman | 28.9.58 | 1/8-1/256 | Dairy B Past. | 1/1 |
| 6 | 32 | M | Greyhound trainer | 1.10.58 | 1/8-1/512 | Raw | 0 |
| 7 | 53 | F | Housewife | 3.10.58 | 1/512 | Dairy A Past. | 0/1 |
| 8 | 26 | M | Cashier | 3.10.58 | 1/256 | Dairy C Past. | 0 |
| 9 | 28 | M | Travelling salesman | 4.10.58 | 1/8-1/256 | Dairy E Past. | 0/1 |
| 10 | 41 | M | Clerk | 5.10.58 | 1/256 | Dairy C Past. | 0/1 |
| 11 | 54 | M | Clerk | 8.10.58 | 1/8-1/256 | Dairy A Past. | 0/2 |
| 12 | 43 | F | Housewife | 8.10.58 | 1/16-1/512 | Dairy A Past. | 0/3 |
| 13 | 53 | M | Clerk | 10.10.58 | 1/8-1/128 | Dairy A Past. | 0/2 |
| 14 | 65 | M | Retired joiner | 18.10.58 | 1/256 | Dairy A Ster. | 0/1 |
| 15 | 48 | M | Plasterer | 24.10.58 | 1/256 | Dairy D Past. | 0/4 |
| 16 | 29 | M | Steelworks cleaner | 17.11.58 | 1/8-1/256 | Dairy C Past. | 0/8 |

five weeks. As the spread was so great it seems improbable that the infection was the result of a single episode but that a continuing factor or factors were operating.

Symptomatology

The symptoms of Q fever are usually remarkably constant (Derrick, 1937; Harman, 1949; Manderson, 1949; Gear, 1955). Those of the Cardiff cases were typical, on the whole. In most patients the onset was sudden. Four patients struggled on for several days but the others retired to bed at the outset. Although headaches in Q fever are described as severe and often retro-orbital, in our series this was not the case. Anorexia was common to all, but apart from nausea and vomiting in 3 patients in the early stages, none had gastro-intestinal symptoms. Swinging temperatures up to 103 F. were common. Pains in the back and chest, cough and delirium occurred in most in the first few days. Drenching sweats were marked in 5 patients. All but one developed pneumonia. Illness lasted from two to four weeks except for one patient who was in hospital for eight weeks. There were no deaths.

Radiologically all had either a segmental or a diffuse patchy consolidation in both lung fields. The diagnosis was by serology in all cases. In none was it possible to fix an incubation period.

Penicillin was given to most cases initially but proved ineffective; all, however, responded to chloramphenicol or Terramycin.

Epidemiology

Each patient and his contacts were interrogated at least twice so that it was possible to get corroborative evidence and to develop a fairly accurate picture of the outbreak.

Milk supply.—Table I shows that only 2 patients drank raw, 13 pasteurized and 1 sterilized milk. The pasteurized milk came from 6 plants between which there had been no interchange. During September, 52 samples of pasteurized milk from Dairy A passed the phosphatase test and 7 samples of sterilized milk had passed the turbidity test. This dairy had had no failures for eight years. The time/temperature charts showed that the milk had

been pasteurized in this dairy at 162 F. to 164 F. during September. 6 samples from Dairy B, 10 from C, 4 from E and 6 from F had been taken and all had passed the phosphatase test during this month.

None of the patients drank much milk and several did not even take it in tea.

Food including other dairy products.—No common article could be found.

Contact with domestic ruminants.—None admitted contact with cattle, sheep or goats within a month of their illness. Patients 3 and 5 visited farms where positive herds had been found in 1956 (Evans). Case 7 worked in a fried fish shop near the cattle market which was visited regularly by farmers. One Rumney dairy farmer called daily. No connexion was found between the remaining cases and domestic or wild animals other than pets.

Pets.—The patients owned 5 dogs, 3 cats, 5 budgerigars and 4 chinchillas. One dog was said to have had ticks, but none roamed the fields. Boiled horse meat was fed to Case 6's greyhounds and one other dog.

Other possibilities.—Straw (Robbins *et al.*, 1946; Wegmann, 1948) and packing (Harvey *et al.*, 1951) have been associated with Q fever. 4 of the Cardiff cases (2, 6, 14 and 15) lived or worked on a new estate where straw and other packing materials were abundant. Case 7's chinchillas were bedded in straw. Rats and mice were not present in the patients' homes.

As investigations proceeded it became clear

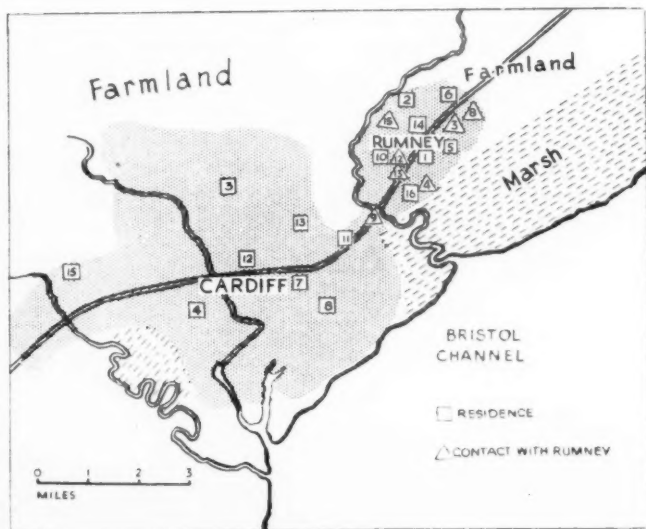


FIG. 1.

that all the cases, either through residence or place of work, or through visiting, were associated with one part of Cardiff—the suburb of Rumney and the adjacent area around the mouth of the Rumney River (Fig. 1). The topography of Rumney is unusual. It is a rapidly growing, purely residential area bounded on the north and east by undulating pasture and on the south by flat marshy land. It is joined to Cardiff by only one road about 1 mile long, traversing marshy ground on which no houses but a few storage depots and garages have been built.

In order to narrow the field of investigation it now became necessary to initiate enquiries in several different directions. It was essential to determine whether the outbreak was part of a larger wave of infection in which the majority of cases were either subclinical or unrecognized. Blood donor serum taken two months before to two months after the outbreak was tested (Table II). Of the 585 donors from Cardiff,

sibility of biting insects is supported by two pieces of circumstantial evidence. The residents of Rumney complained of a plague of biting insects, supposedly mosquitoes, in the first three weeks of September. This was sufficiently unpleasant to be recorded several times in the local newspapers and to have come to the attention of the local authorities. The casualty department of the local hospital reported many cases of septic insect bites at this time. One of us (A. D. E.) has seen several examples of *Culex molestus* which were caught at the time. For the whole of September the wind blew from the south or south-east—unusual directions for Cardiff. This might account for the prevalence of mosquitoes in Rumney as the lands lying to the south and south-east are ideal mosquito breeding grounds.

As autumn calving was common in the district it is probable that a rich source of *R. burneti*, in infected placentas and birth membranes, was

TABLE II.—Q FEVER ANTIBODIES IN THE SERA OF BLOOD DONORS IN S. WALES IN AUGUST–DECEMBER 1958

| | | Serum C.F. titres | | | | | Total | Percentage positive |
|----------------|----------|-------------------|------|------|-------|----------|-------|---------------------|
| | | 1/16 | 1/32 | 1/64 | 1/128 | Negative | | |
| August 1958 | S. Wales | 9 | 3 | 0 | 1 | 524 | 537 | 2.5 |
| | Cardiff | 3 | 0 | 0 | 0 | 105 | 108 | 2.8 |
| September 1958 | S. Wales | 17 | 0 | 2 | 1 | 471 | 491 | 4.0 |
| | Cardiff | 1 | 1 | 0 | 1 | 92 | 95 | 3.2 |
| October 1958 | S. Wales | 22 | 1 | 1 | 0 | 636 | 660 | 3.7 |
| | Cardiff | 3 | 1 | 0 | 0 | 114 | 118 | 3.4 |
| November 1958 | S. Wales | 18 | 2 | 1 | 0 | 664 | 685 | 3.1 |
| | Cardiff | 2 | 0 | 1 | 0 | 146 | 149 | 2.1 |
| December 1958 | S. Wales | 17 | 2 | 0 | 1 | 490 | 510 | 3.9 |
| | Cardiff | 2 | 0 | 0 | 1 | 112 | 115 | 2.7 |
| Total: | S. Wales | 83 | 8 | 4 | 3 | 2,785 | 2,883 | 3.4 |
| Total: | Cardiff | 11 | 2 | 1 | 2 | 569 | 585 | 2.8 |

71 lived in Rumney. Only 3 of these had complement-fixation titres of 1/16 and none had greater. This suggested that the outbreak was restricted in extent, that the source of infection should be sought in Rumney and that the outbreak was not milk-borne. Confirmation was obtained by examination of the blood of the family contacts. Only 1 showed evidence of recent Q fever (Table I).

68 milk samples from local farms are being tested for *R. burneti*. The veterinary surgeon who collected these enquired about the health of the animals and of the farmer and his family and staff, the distribution of milk and undue prevalence of insects. Apart from confirmation that autumn calving was common, nothing of significance was revealed. Ticks were not found and it was said that mosquitoes had been abundant.

Two types of insects as the means of spread of infection must now be considered. The pos-

sibility of biting insects is supported by two pieces of circumstantial evidence. The residents of Rumney complained of a plague of biting insects, supposedly mosquitoes, in the first three weeks of September. This was sufficiently unpleasant to be recorded several times in the local newspapers and to have come to the attention of the local authorities. The casualty department of the local hospital reported many cases of septic insect bites at this time. One of us (A. D. E.) has seen several examples of *Culex molestus* which were caught at the time. For the whole of September the wind blew from the south or south-east—unusual directions for Cardiff. This might account for the prevalence of mosquitoes in Rumney as the lands lying to the south and south-east are ideal mosquito breeding grounds.

As autumn calving was common in the district it is probable that a rich source of *R. burneti*, in infected placentas and birth membranes, was present in the farm lands so that contamination of the patients' food could have occurred by non-biting insects. This possibility, too, is strengthened by the knowledge of the direction of the wind at the time.

Philip (1948) found that *Aedes aegypti* ingested *R. burneti* when they were fed on infected guinea-pigs, but could not transmit the infection to other guinea-pigs immediately afterwards or at intervals up to 30 days. *R. burneti* did not persist in the mosquitoes for more than three days. Despite this evidence we intend to carry out a survey of mosquitoes and other biting insects in the Rumney area and to try transmission experiments under laboratory conditions.

Summary

An outbreak of Q fever, affecting 14 men and 2 women, in a suburb of Cardiff in autumn 1958 is described. Detailed investigations failed to reveal the mode of spread, but the

possibility of mosquito-borne infection is being examined.

Acknowledgments.—We wish to acknowledge the assistance of the following in the collection of materials and data and in the preparation of this paper: Drs. R. Drummond, W. Powell Phillips, A. H. Griffith, W. B. Clarke, R. D. Grey, Messrs. A. C. Beynon, M.R.C.V.S., D.V.S.M., D. C. Davies, M.R.C.V.S., D.V.S.M., I. James, H. C. Bird, W. Bate; and Mrs. J. M. Jones and Mr. R. Marshall for the preparation of the illustration.

REFERENCES

- BABUDIERI, B. (1953) *W.H.O. Monograph Series*, No. 19, 157.
- BURNET, F. M., and FREEMAN, M. (1937) *Med. J. Aust.*, ii, 299.
- BELL, J. A., BECK, M. D., and HUEBNER, R. J. (1950) *J. Amer. med. Ass.*, **142**, 868.
- CAMINOPETROS, J. (1948) *Int. Congr. Trop. Med.*, **4**, 33.
- CLARK, W. H., BOGUCKI, A. S., LENNETTE, E. H., DEAN, B. H., and WALKER, J. R. (1951) *Amer. J. Hyg.*, **54**, 15.
- DAVIS, G. E., and COX, H. R. (1938) *Publ. Hlth Rep. Wash.*, **53**, 2259.
- DERRICK, E. H. (1937) *Med. J. Aust.*, ii, 281.
- (1944) *J. Hyg., Camb.*, **43**, 357.
- (1953) *Med. J. Aust.*, i, 245.
- EVANS, A. D. (1956) *Mon. Bull. Minist. Hlth Lab. Serv.*, **15**, 215.
- GEAR, J. (1955) *Lancet*, ii, 1167.
- HARMAN, J. B. (1949) *Lancet*, ii, 1028.
- HARVEY, M. S., FORBES, G. B., and MARMION, B. P. (1951) *Lancet*, ii, 1152.
- HUEBNER, R. J., and BELL, J. A. (1951) *J. Amer. med. Ass.*, **145**, 301.
- KAPLAN, M., and BERTAGNA, P. (1955) *Bull. Wld Hlth Org.*, **13**, 829.
- MACCALLUM, F. O., MARMION, B. P., and STOKER, M. G. P. (1949) *Lancet*, ii, 1026.
- MANDERSON, W. G. (1949) *Lancet*, ii, 1085.
- MARMION, B. P., and STOKER, M. G. P. (1956) *J. Hyg., Camb.*, **54**, 547.
- (1958) *Brit. med. J.*, ii, 809.
- , MCCOY, J. H., MALLOCH, R. A., and MOORE, B. (1953) *Lancet*, i, 503.
- MURDOCK, C. R. (1959) Personal communication.
- PHILIP, C. B. (1948) *J. Parasit.*, **34**, 347.
- Report to Public Health Laboratory Service. (1956) *Mon. Bull. Minist. Hlth Lab. Serv.*, **15**, 10.
- ROBBINS, F. C., GOULD, R. L., and WARNER, F. B. (1946) *Amer. J. Hyg.*, **44**, 23.
- SLAVIN, G. (1952) *Vet. Rec.*, **64**, 743.
- STOKER, M. G. P. (1949) *Lancet*, i, 178.
- SYRUCZEK, L., and RASKA, K. (1956) *Bull. Wld Hlth Org.*, **15**, 329.
- WEGMANN, T. (1948) *Schweiz. med. Wschr.*, **78**, 529.
- WELSH, H. H., LENNETTE, E. H., ABINANTI, F. R., and WINN, J. F. (1958) *Ann. N.Y. Acad. Sci.*, **70**, 528.

DISCUSSION

Dr. L. Syrucek (Prague):

Q Fever in Western Czechoslovakia

Q fever in man was first observed in Czechoslovakia in 1952; the infections were confirmed serologically in 1953 and by isolation of the organism in 1954 (Patočka and Kubelka, 1953; Raska *et al.*, 1954). The first observations were made in a hilly and sparsely inhabited region of western Bohemia where the population consisted of two distinct groups—a native German farming population and a recently settled population of Czech and Slovak immigrants, also mostly farmers. In 1953 and 1954 severe outbreaks of Q fever occurred in the human population, notably in two villages where between 55% and 82% of the adults were infected. Large herds of cows were kept in both villages and nearly 1,000 sheep in one of them. These domestic ruminants were proved by epidemiological investigation and by isolation and serological tests to be the source of the human infection. It was concluded that Q fever in this area was a recently imported infection after the Second World War for the following reasons: (1) In both villages the slaughter-house employees, veterinary and dairy workers and all concerned with the infected herds, carcasses and products, were found to be serologically negative in 1953. During 1954 they became gradually infected and in 1955 a significant rise in antibodies against Q fever antigen was observed in most of them. (2) The infection spread equally among both groups of the population—the indigenous and recent immigrants. (3) The attack rate was unusually high in both man and

animals. (4) From 1954 to 1956 the infection spread gradually from farm to farm. (5) From 1948 to 1950 Roumanian sheep were imported into this particular region in hundreds and during these same years Q fever was very prevalent among sheep in Roumania, as stated by Combiescu and other Roumanian authors.

Having shown that *R. burneti* was excreted by the infected ruminants, and knowing the wide range of susceptible animals, we decided to investigate the spread of Q fever in wild life in the epidemic area. We began by studying serologically and by isolation both natural and experimental infections in wild mammals and birds. In 1954, 1955 and 1956 we found evidence of infection with *R. burneti* in various domestic mammals and birds and in various species of rodents, insects and birds in the vicinity of pastures used by the infected sheep and cattle (Syrucek and Raska, 1956).

We were concerned to find out whether this infection would persist in the area or spread further—as do, for example, tickborne encephalitis, tularemia or plague—or whether it would die out owing to unsuitable ecological and climatic conditions. We therefore kept these two villages under observation in 1957 and 1958. Our findings showed a progressive decline of infection in man and in both domestic and wild animals. The number of persons with clinical evidence of Q fever confirmed by laboratory test was 11 in 1952, 37 in 1953, 57 in 1954 and then, apart from 4 in 1956, no more were found. Some results are given in Table I.

TABLE I.—RESULTS OF SEROLOGICAL EXAMINATION OF SOME DOMESTIC AND WILD ANIMALS 1954-1958

| Year | Cows | | Hens | | Rodents | | Wild birds | |
|------|----------|----------|----------|----------|----------|----------|------------|----------|
| | Examined | Positive | Examined | Positive | Examined | Positive | Examined | Positive |
| 1954 | 170 | 94 | 61 | 12 | 193 | 4 | 138 | 19 |
| 1955 | 91 | 15 | n.d. | — | 182 | 9 | 124 | 2 |
| 1956 | 105 | 20 | n.d. | — | 452 | 27 | 77 | 5 |
| 1957 | 273 | 30 | n.d. | — | 387 | 6 | 22 | 0 |
| 1958 | 147 | 0 | 48 | 0 | 74 | 0 | n.d. | — |

n. d.—no data

It will be seen that as soon as the original source of infection in ruminants ceased, Q fever in wild life disappeared. This finding is in contrast to the results of Australian and Russian workers who found the wild life infected in regions where no domestic animals were involved and where one must therefore presume the infection to have been a primary and persistent one. Differences of climatic and ecological factors may explain this. Owing to the cold climate of Western Czechoslovakia there are no ticks in the area we observed and this might be one of the reasons why Q fever disappeared. This

would correspond with the opinions of Terhaag and other workers in Germany and America, who sought to prove the importance of ticks in the endemicity of Q fever.

It would seem that Q fever can only be endemic in areas where both ticks and mammalian hosts abound—the latter being either domestic ruminants pastured in the open, or susceptible rodents and perhaps other wild animals. These conditions are not present in Western Czechoslovakia and this may account for Q fever dying out in the areas mentioned. This may be analogous to the appearance of plague in wild rodents in East Anglia in 1908 and its disappearance after 1918.

REFERENCES

- PATOCKA, F., and KUBELKA, B. (1953) *Csl. Epidem., Mikrobiol., Immunol.*, **2**, 340.
 RASKA, K., ALDOVA, E., KUBASEK, M., SYRUCER, L., HAVLIK, O., MANYCH, J., and SANA, B. (1954) *Cas. Lek. ces.*, **93**, 1153.
 SYRUCER, L., and RASKA, K. (1956) *Bull. Wild Hlth Org.*, **15**, 329.

Meeting

May 4, 1959

Professor JONAS E. SALK (Pittsburgh) presented a paper entitled **Vaccination against Poliomyelitis—How Much is Enough?**

Dr. D. G. EVANS and Dr. F. O. MACCALLUM opened the subsequent discussion.

Meeting

May 22, 1959

Review of Morbidity Among Young Soldiers [Summary]

By S. ROSENBAUM, M.A.

Army Medical Department

THE health of young soldiers has been reviewed over a seven-year period, from 1950 to 1956, when the conditions of National Service and the structure of the Army were fairly stable. National Service covered the fittest 80% of the young male population of the country and the Army took over two-thirds of those recruited; the consequences of soldiering were therefore important to the health of the nation.

Geographical and climatic differences in the places where they served were found to have greater influence on their health during the period studied than differences from year to year, although decided improvements were recorded between the beginning and end of the seven years in many diseases.

Injuries are a major preventable source of wastage and one where the soldier runs his own occupational hazards, especially in time of war. Injuries formed about one-eighth of all admissions to a medical unit for more than forty-eight hours. The main health problems other than injuries can be seen by listing those admission rates that amounted to 1% of strength or more when averaged over the seven years. Table I,

apart from the United Kingdom, is restricted to the three main overseas commands: British Army of the Rhine, Middle East Land Forces and Far East Land Forces.

TABLE I.—DISEASES WITH AN AVERAGE ADMISSION RATE OF 1% OF STRENGTH OR MORE
Admission Rates per 1,000 Averaged over 1950-1956

| | UK | BAOR | MELF | FARELF |
|-----------------------------|-----|------|------|--------|
| Respiratory diseases .. | 88 | 46 | 46 | 42 |
| Otitis externa and media .. | | | 10 | 16 |
| Skin diseases .. | 33 | 42 | 52 | 74 |
| Venereal diseases* .. | | 14* | 16* | 98* |
| Intestinal diseases .. | | | 66 | 40 |
| P.U.O. .. | | | 21 | 20 |
| Malaria .. | | | | 9 |
| All diseases .. | 261 | 241 | 329 | 458 |

*These figures also include patients not admitted.

Clearly the respiratory diseases stand out in the United Kingdom and skin conditions in the Far East, where, if it were not for venereal diseases, they would be the leading cause. Venereal diseases are in a special category as every single case during this period was counted whether admitted as an in-patient or not, and they therefore have an enhanced prominence in the morbidity tables beyond their true importance.

Apart from venereal diseases Far East rates only exceeded the Middle East to any degree in skin conditions. These were of great importance in all commands and were largely governed by the group of septic conditions such as boils which averaged about 21 per 1,000 in the European commands and 32 per 1,000 in the tropical commands. The principal addition in the Far East was from tinea, which was uncommon elsewhere, but there reached one-fifth of all skin conditions. Even this conceals its widespread extent, for large numbers were treated at medical centres as out-patients.

Intestinal diseases have been of greatest concern in the Middle East where they dominated the medical scene from May to October. The largest and yet the mildest group was the somewhat amorphous one of diarrhoea, enteritis, &c., with an average treatment of about a week. A detailed examination of in-patient records shows that the great majority in the United Kingdom were diagnosed as gastro-enteritis and colitis, fairly evenly spread throughout the year, while in the Middle East this category was in the minority. The diarrhoea group may well include unidentified cases of dysentery. Enteric fever should be mentioned as the only one of the intestinal group against which protection is

sought by the universal use of a vaccine, and possibly it is this which at times has brought it within bounds while the other intestinal diseases remained rampant. At any rate, by 1951 it had reached a record low post-war level in the Middle East (there were too few cases elsewhere to be worth discussing). Subsequently outbreaks of paratyphoid B occurred until the Suez Canal zone was evacuated.

The younger soldiers had the higher admission rates, but in the United Kingdom age was a subordinate factor in determining morbidity, which was largely shaped by length of service. The recruit stage was particularly vulnerable in respect of respiratory conditions. A similar factor came into play after arrival in the tropical commands, on being exposed to another new environment.

There appeared to be an advantage in a later call-up; recruits whose service had been deferred had lower admission rates, possibly due to their healthier home background. Recruits whose service had been deferred have previously been shown to differ in respect of physique also (Rosenbaum, 1954).

REFERENCE

ROSENBAUM, S. (1954) *J. R. statist. Soc., Ser. A*, **117**, 331.

DISCUSSION

Wing Commander R. J. A. Morris: From what Mr. Rosenbaum has told us it would seem that the health of young men in the Army follows the same general pattern as that of young airmen. There are, of course, certain risks peculiar to each of the Services. Although, since 1951, the Forces have used common inter-service documents for recording much of the information from which their medical statistics are derived, great care should be taken when attempting to compare published figures unless terms and methods of compilation are fully defined. For example, R.A.F. figures for admission to hospital or sick quarters generally include all reported sickness at home or elsewhere while on leave or pass. It is understood that this is not so in the Army.

As "sickness-at-home" comprises one-third of all R.A.F. admissions in the United Kingdom, due allowance for this should be made when considering figures, especially for certain disease groups. In 1956 Acute Upper Respiratory Infections (A. 87 and 88) accounted for over 44% of all "sickness-at-home", and of all R.A.F. admissions from this cause, 39% occurred in personnel "sick-at-home". The mean admission rate for Acute Upper Respiratory Infection (A. 87 and 88) in the R.A.F. in the United Kingdom for 1950-56 was 140 per 1,000, whereas the Army

rate for respiratory infections, quoted by Mr. Rosenbaum, was only 88 per 1,000; however, after a 39% reduction for "sickness-at-home", the R.A.F. rate becomes 85 per 1,000. Presuming that Army and R.A.F. personnel suffer a similar amount of "sickness-at-home", the total admission rate for the Army is likely to be not 261 per 1,000, as stated, but nearer 430 per 1,000 which accords more closely to R.A.F. experience (405 per 1,000). Thus, to assess total morbidity in the Services, the effect of "sickness-at-home" must be included.

The R.A.F. experience of the effect of age on sickness is much the same as the Army's, the highest rates occurring in the younger age groups. In 1956 the admission rate for persons less than 20 years of age was 1.7 times that for all ages, while that for recruits in their first eight weeks of service was over twice the general rate. That this was not entirely due to age is illustrated by the fact that the rate for Apprentices and Boy Entrants was only 1.4 times the total rate.

Much of the increased sickness in recruits is attributable to the high rates of upper respiratory infection that occur in communities herded together for the first time. Here the adenovirus plays a large part, as was shown by McDonald *et al.* (1958) who also indicated the serious after-effects of respiratory infections at recruit centres.

Although recruit training occupies less than a twelfth of an airman's service, respiratory infection incurred during this period accounted for over half the invalidings due to respiratory disease.

REFERENCE

- MCDONALD, J. C., WILSON, J. S., THORBURN, W. B., HOLLAND, W. W., and ANDREWS, B. E. (1958) *Brit. med. J.*, ii, 721.
- Surgeon Commander F. P. Ellis:** I would like to refer to one aspect raised by Mr. Rosenbaum's paper only, namely the effect of climate on the morbidity of military personnel. The Royal Navy was particularly concerned with this aspect in the latter years of the Second World War when accurate information was difficult to obtain because the Annual Reports on the Health of the Navy and the machinery for producing them had been discontinued and ships' medical officers, for reasons of security, were not allowed to report the movements of their ships. An attempt was made in 1944 and 1945 to obtain some factual data from the Eastern Fleet and the British Pacific Fleet. All medical officers were instructed to report the total numbers of fresh cases on the "sick" and "attending" lists in certain broad disease groups for each month a ship had been in the tropics, and for the previous twelve months for shore establishments. A marked contrast was observed in both Fleets in total sickness between the shore establishments and the ships. An increase in skin diseases and minor injuries afloat, where the average dry-bulb temperature in the accommodation between decks was about 7° F. in excess of the average temperature in the accommodation on shore, accounted for most of the additional morbidity (Ellis, 1948).
- After the war it was possible to request information concerning the movements of ships, and for the first post-war year the average attending-list and sick-list figures derived from reports from all ships in the Navy were presented by Fraser Roberts (1948) for northern, southern, Mediterranean and tropical waters. His figures were based on the weekly sickness rates calculated by taking the average for the figures for sickness at the beginning and end of each week and dividing by the similarly averaged complement. They showed very much the same trends as Mr. Rosenbaum describes for Germany, the Middle East and the Far East, namely an increase in morbidity as one goes East. The contrasting prominence of upper respiratory tract infections in temperate zones to which Mr. Rosenbaum refers was not indicated by these figures from ships, although I suspect that if naval shore establishments, especially training establishments and barracks, had been included the story might have been different. As in the Army, "dysenteries and diarrhoeas" were a more prominent cause of morbidity in the Mediterranean than in either the tropical or temperate zones. Sickness due to injuries was more prominent in the warm climates than the temperate climates and skin diseases were far and away the most frequent cause of morbidity in the tropics.
- Medical officers were then instructed to include the average weekly upper-deck temperature at noon in their monthly returns. For the first year for which returns were received—October 1, 1948, to September 30, 1949—the effect of climate on total morbidity was shown by the attending-list figures which rose appreciably when the mean weekly noon upper-deck dry-bulb temperature exceeded 80° F. and very markedly when it exceeded 90° F. (Ellis *et al.*, 1953). Little was to be learnt concerning the effects of climate from the sick-list figures alone.
- To confirm the critical level of warmth at which morbidity increased, this study was continued and the findings for the four-year period October 1948 to September 1952 were recently reported by Smith (1958). In view of the apparent insensitiveness of the sick list as a criterion for measuring climatic effects in the preliminary study, he confined his attention largely to the attending list. The disease groups chosen for study again correspond broadly to those selected by Mr. Rosenbaum. The percentage of the ships' companies on the attending list, particularly with skin diseases, increased when the average upper-deck dry-bulb temperature at noon exceeded 80° F., which had been shown in another study to correspond approximately to an average effective temperature on the mess decks of about 80° F. This trend of increasing morbidity at climatic extremes was less marked at the lower end of the temperature scale.
- These studies provided the Admiralty with useful evidence, in support of that obtained by "comfort" surveys and physiological and psychological studies, bearing on the necessity for air-conditioning warships to maintain the effective temperature between decks below 78° F. if they are required for continuous service in the tropics, and suggested that any complete review of morbidity in the Service should include figures for the attending list as well as for the sick list if useful information was not to be lost and significant trends ignored.

REFERENCES

- ELLIS, F. P. (1948) *Brit. med. J.*, i, 587.
 —, SMITH, F. E., and UNDERWOOD, C. R. (1953) *Brit. J. prev. soc. Med.*, 7, 69.
 ROBERTS, J. A. F. (1948) *Brit. J. soc. Med.*, 2, 55.
 SMITH, F. E. (1958) *Brit. J. industr. Med.*, 15, 197.

BOOKS RECEIVED FOR REVIEW

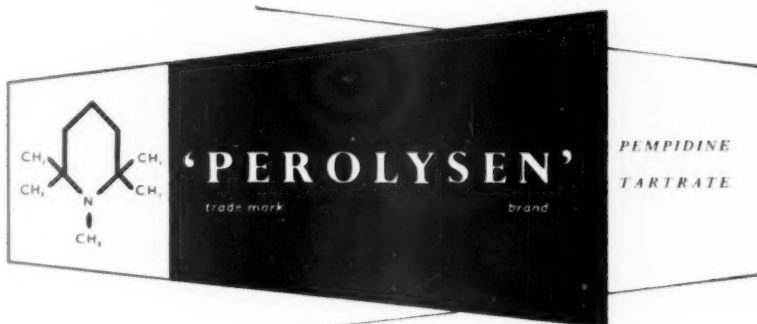
- Bailey (H.), and Bishop (W. J.).** Notable names in medicine and surgery. 3rd. ed. pp. xiii + 216. London: H. K. Lewis. 35s. 1959.
- Bourne (A.).** A synopsis of obstetrics and gynaecology. 12th ed. pp. vii + 632. Bristol: John Wright and Sons. 35s. 1959.
- Brodal (A.).** The cranial nerves. Translated from the Norwegian by the author. pp. 141. Oxford: Blackwell. 15s. 1959.
- Cecil (R. L.), and Loeb (R. F.), eds.** A textbook of medicine. 10th ed. pp. xxxiii + 1664 + lxxxix. Philadelphia and London: Saunders. £5 15s. 6d. 1959.
- C.I.O.M.S.** Methods of geographical pathology. Report of the study group convened by the Council for International Organisations of Medical Sciences. Edited by R. Doll. pp. 72. Oxford: Blackwell. 9s. 6d. 1959.
- Crawford (J. S.).** Principles and practice of obstetric anaesthesia. pp. 128. Oxford: Blackwell. 20s. 1959.
- Cruikshank (A. G.), and Stewart (C.).** A pocket book of proprietary drugs. pp. 236. Edinburgh and London: Livingstone. 10s. 6d., interleaved copy 14s. 1959.
- Cumings (J. N.).** Heavy metals and the brain. pp. vii + 161. Oxford: Blackwell. 32s. 6d. 1959.
- Davidson (Sir S.), Meiklejohn (A. P.), and Passmore (R.).** Human nutrition and dietetics. pp. xii + 844. Edinburgh and London: Livingstone. 84s. 1959.
- Dowling (H. F.), and Jones (T.).** That the patient may know. An atlas for use by the physician in explaining to the patient. pp. xiii + 139. Philadelphia and London: Saunders. 52s. 6d. 1959.
- Evrard (E.), Bergeret (P.), and van Wulfften Palthe (P. M.), eds.** Medical aspects of flight safety (the unexplained aircraft accident). pp. ix + 308. Published for Advisory Group for Aeronautical Research and Development, NATO. London: Pergamon Press. 80s. 1959.
- Hennessy (T. G.), et al., eds.** Radiobiology at the Intra-cellular level. Proceedings of the first U.C.L.A. Conference on Radiobiology held at Catalina Island, September 9-12, 1957. pp. x + 208. London: Pergamon Press. 60s. 1959.
- Jepson (R. P.), and Catchpole (B. N.).** An introduction to surgery for dental students. pp. x + 166. London: English Universities Press. 21s. 1959.
- Lee (J. A.).** A synopsis of anaesthesia. 4th ed. pp. 616. Bristol: John Wright and Sons. 27s. 6d. 1959.
- McMenemey (W. H.).** The life and times of Sir Charles Hastings. pp. xii + 516. Edinburgh and London: Livingstone. 50s. 1959.
- Martmer (E. E.), ed.** The child with a handicap. A team approach to his care and guidance. pp. xxiv + 409. Springfield, Ill.: Thomas; Oxford: Blackwell. 82s. 6d. 1959.
- Monro (P. A. G.).** Sympathectomy. An anatomical and physiological study with clinical applications. pp. xx + 290. London: Oxford University Press. 75s. 1959.
- Mündnich (K.), and Frey (K.-W.).** Das Röntgenschnittbild des Ohres: The tomogram of the ear (in English and German): pp. xii + 123. Stuttgart: Thieme. DM. 66. 1959.
- Mushin (W. W.), Rendell-Baker (L.), and Thompson (P. W.).** Automatic ventilation of the lungs. pp. xvi + 349. Oxford: Blackwell. 47s. 6d. 1959.
- Peterson (J.).** Children in practice. pp. vii + 226. London: Cambridge University Press. 25s. 1959.
- Pitt-Rivers (R.), and Tata (J. R.).** The thyroid hormones. pp. xiii + 247. London: Pergamon Press. 50s. 1959.
- Prunty (F. T. G.), McSwiney (R. R.), and Hawkins (J. B.).** A laboratory manual of chemical pathology. pp. ix + 260. London: Pergamon Press. 35s. 1959.
- Roberts (J. A. Fraser).** An introduction to medical genetics. 2nd. ed. pp. x + 263. London: Oxford University Press. 35s. 1959.
- Ross (E. J.), ed.** Clinical effects of electrolyte disturbances. The Proceedings of a Conference held in London at the Royal College of Physicians of London, February 27-28, 1959. pp. x + 210. London: Pitman. 20s. 1959.
- Ross (S. T.).** Synopsis of treatment of anorectal diseases. pp. 240. St. Louis: C. V. Mosby Company; London: Henry Kimpton. 48s. 6d. 1959.
- Schorn (J.).** Zur Orthologie und Pathologie der Hoyer-Grosser'schen Organe. No. 6 of Zwanglose Abhandlungen aus dem Gebiet der normalen und pathologischen Anatomie. pp. 88. Stuttgart: Thieme. 1959.
- Squires (H. C.).** The Sudan Medical Service. An experiment in social medicine. pp. xii + 138. London: Heinemann. 15s. 1958.
- van der Plaats (G. J.).** Medical X-ray technique. Principles and practice. Translated by G. E. Luton. pp. xii + 480. Eindhoven: Philips' Technical Library. 57s. 6d. 1959.

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Section of General Practice

President—G. J. V. CROSBY, C.B.E., M.D.

Meeting

January 21, 1959

DISCUSSION ON IRREGULAR UTERINE HÆMORRHAGE [Summary]

Dr. E. D. Forster (Matlock):

The problems raised under this heading, as in all obstetrics and gynaecology, are inescapable by any family doctor. His own principal interests may lie elsewhere; but these are subjects whose scientific aspects are outweighed by their emotional and human associations; they comprise matters which concern far more than the womenfolk, and which may affect the whole of family life. Problems of marital relation, of contraception, of therapeutic sterilization and abortion are of vital importance to the patient, and to her family background; and they may involve the doctor in legal, ethical, philosophical and religious problems, for which little provision has been made in his syllabus of instruction. Some departments of medicine the family doctor may, if he wishes, leave alone; or when they concern his patients, he may delegate them; but obstetrics and gynaecology, which permeate and integrate his work, he cannot escape. Apart from the importance of their social and family association, the scientific aspect can be of crucial importance. Certain fairly simple sign-symptom patterns may have a trivial basis, or else connote dangerous disease. The consultant, with his special knowledge, experience and equipment, stands ready to deal with difficulties as they arise. The burden and the responsibility of the sorting process must lie with the general practitioner. The responsibility is a heavy one, and the sorting by no means as easy as some might suppose. The very nature of his work subjects him to constant and diverse calls upon his attention—many tugs on the alarm cord, but a number of the alarms are false.

To conserve a continual wariness, and to maintain a look-out for danger is a plain duty, but a duty not always easy to perform. Irregular uterine bleeding provides a case in point. Bleeding is a normal uterine function, and minor irregularities of no serious import frequently occur. The subject is a delicate one to many women, and they are not always prompt to report their troubles, or candid when they bring themselves to do so. Language can be a barrier to obstruct, as well as a means to further, communication.

The difficulties faced by the family doctor make

it the more important that a friendly relationship should be forged between himself and his consultant colleagues; and that the latter should be always ready to lend the weight of their special experience, with a sympathetic understanding of his dilemmas, in support of the man in the front line.

Mr. Aleck Bourne (London):

As the subject is too wide for a complete discussion I shall limit myself to the clinical types of puberty, metropathia, the menopause and after, and prolonged shedding at menstruation.

Puberty

A minority of girls suffer from irregular, excessive and prolonged bleeding at the initiation of menstruation which causes anæmia, fatigue, apathy and anxiety. It is due to a confused evolution of the pituitary-ovarian relation whereby there is an alternating excess or deficiency of secretion of follicular oestrogen and no development of the corpus luteum. Of Sutherland's 200 cases (1953) there was an organic pathology in 53 (26.5%), as follows: Chronic endometritis in 10, hyperplasia (metropathia) in 31, endometrial tuberculosis in 8, and endometrial atrophy in 4.

Treatment.—Mild cases react to rest from school and examinations, iron, high-protein feeding and milk (for its absorbable calcium). Trial may be made of stilbæstrol (1 or 2 mg. daily), or ethisterone (25 mg. by mouth) if stilbæstrol fails after a few days' treatment. If after a short trial there is no improvement, or bleeding is really severe with anæmia, the patient should be curetted and the whole of the scrapings examined microscopically. This is necessary in view of the relatively high percentage of organic changes as shown by Sutherland. Curettage may cure or give a lead to specific treatment.

Metropathia (Cystic Glandular Hyperplasia)

The endometrium is thickened and often polypoid by dilatation and cellular proliferation of the glands and vascular congestion of a dense

stroma. The cystic glands may be large enough to be visible to the naked eye. One ovary contains a large unruptured follicular cyst and corpora lutea are absent. The *cause* is a failure in the alternating rhythm of the pituitary secretion of the follicle-stimulating and luteinizing gonadotrophins which interferes with the corresponding development of the graafian follicle and corpus luteum. Prolonged oestrogen therapy will produce exactly the same endometrial changes. The underlying cause may often be traced to an emotional stress. The *symptom* is hæmorrhage which is irregular in incidence, duration and amount. It may last for weeks and occasionally be quite severe but it may cease for as long as six or eight weeks. Vaginal examination may find nothing definite but sometimes an enlarged cystic ovary on one side and mild uniform enlargement of the uterus may be felt.

Diagnosis.—Malignant disease of the cervix and corpus must be excluded by the curette and microscope. Fibroids are usually easily noticed by the irregular uterine outline but the intra-uterine fibroid polypus or small submucous fibroid may be impossible to determine even by dilatation and curettage. However, a fibroid polypus will cause almost continuous or steady bleeding but not so severe as that of metropathia nor will there be long intervals without bleeding. The doubt can be settled by anterior vaginal hysterotomy which opens the internal os enough for digital palpation of the uterine cavity.

Treatment.—It is important to uncover any emotional stress and, if present, to alleviate it by the help of a psychiatrist. A severe bout of hæmorrhage may be arrested in a few hours by giving large doses of stilbæstrol (5 mg.) every two hours until the bleeding stops, but this will be followed in ten days or so by more bleeding—"withdrawal hæmorrhage". For the commoner causes of milder bleeding progesterone (10–20 mg.) may be given intramuscularly for five days. Small short withdrawal bleeding will probably follow in a week. Three weeks after this stops the injections of progesterone should be repeated, and so on for three months. Results are often disappointing. Curettage may regularize the mildest cases and will usually be successful, at least temporarily, if the endometrium is polypoid. Hysterectomy may be necessary especially if the patient is near the menopause.

The Menopause and After

Apart from the minor irregularities and excesses around the ages of 48–50 pathological hæmorrhage of many varieties is common.

Every case must be fully investigated beginning with an enquiry if the patient has been taking stilbæstrol or other oestrogen over a long period. In about one-third of all cases the cause is malignant disease of cervix or corpus. The next common cause is probably cystic hyperplasia of the endometrium (metropathia) due to irregular endocrine involution which, in its turn, induces a high and varying secretion of ovarian oestrogen. Hyperplasia is found not only during the menopause but at any time afterwards up to many years. The ovary may be re-awakened into activity, but when hyperplasia is found after, say, the age of 60 years, the source of the oestrogen is almost certainly the adrenal. These women may have glycosuria and hirsuties. Diagnostic curettage is necessary for every patient complaining of frequent excessive or prolonged hæmorrhage at and after the menopause. All the tissue removed must be examined microscopically. If cystic hyperplasia is found after a period of amenorrhœa the only safe treatment is hysterectomy because of the frequent risk and considerable danger of either a coexisting carcinoma of the endometrium or its later development from the actively proliferating cells of the cystic glands. Common causes of blood staining apart from growths are senile septic vaginitis and cervical mucous polypi. These may be innocent but quite often at this time of life they may contain a microscopic malignant focus.

A rare cause of irregular bleeding which may arise at any time to extreme old age is a feminizing ovarian tumour which secretes oestrogen. As after prolonged stilbæstrol therapy, cystic hyperplasia is inevitable and becomes malignant in as many as 20 to 30% of the cases.

If hyperplasia is found actually at the menopause, methyl testosterone (10 mg. daily) may be tried for not more than two months, after which a second exploratory curette should be done to discover the effect of the hormone.

Prolonged Shedding of the Menstruating Endometrium

Normally the upper half to two-thirds of the endometrium is shed during the first three days of the period after which regeneration begins under the influence of the rising secretion of oestrogen. If regeneration fails as a result of inadequate secretion of oestrogen the free surface of the endometrium remains ragged and bleeding. The "period", therefore, will continue until the level of oestrogen rises to its normal physiological level. There will be bleeding for a few days or several weeks as a continuous mild oozing which no drugs will stop. Diagnosis can only be made by curetting the uterus during the bleeding

episode. Sections will clearly show the unhealed surface of the endometrium.

Treatment.—Stilbæstrol (1 to 3 mg.) or oestradiol (0.1 mg.) daily for a few days will stimulate regeneration and arrest the bleeding. Rather large doses are necessary to overcome the continued secretion of progesterone by a

persistent corpus luteum. Sutherland found an incidence of 4.5% in his 1,000 cases of "functional uterine hæmorrhage" of prolonged shedding and a similar, probably identical condition called "irregular ripening".

REFERENCE

SUTHERLAND, A. M. (1953) *Glasg. med. J.*, **34**, 496.

Meeting

February 18, 1959

DISCUSSION ON THE CONTRIBUTION OF THE GENERAL PRACTITIONER AND THE INDUSTRIAL MEDICAL OFFICER TO THE HEALTH OF THE COMMUNITY

Dr. W. H. Leake (Bradford):

The object of the work of a general practitioner is to give (or see that it is given) the right treatment at the right time and in the right place. His work includes the prevention and treatment of any illness, or injury, affecting the mind or any part of the body whether the patient be in the town or in the depths of the country. The general practitioner should consider himself as the key member of a team working for the benefit of his patients so that lives can be saved by accurate and early diagnosis. He should not be considered by the community as a mere "filler-in of government forms". General practice embraces a wide range of human relationships and since health is intimately related to work, happiness and purpose in life its problem may concern almost anything or anybody; it may be medical or social or both.

During the last fifty years tremendous progress has been made in all branches of medical science and especially noteworthy are the achievements of preventive medicine.

The obstacles to be surmounted in the control of disease are still many but none would venture to predict the limits of future achievements in the "Combined Operations" of medical science against disease. Every branch of medicine has to play its part not only in the prevention and cure of disease but also in the raising of the standards of individual and community health, taking as its motto the well-known quotation, "Life is not living—but living in health" (Martial).

I do not think any general practitioner if he ponders seriously for a few moments can be satisfied or contented about the standards of health of the community at this present age, in spite of the benefits and advantages of the "Welfare State". Let me illustrate this point in a limited sphere with which I am specially

acquainted. From 1946 until a short time ago I have acted as Chairman of No. 1 Medical Board, Ministry of Labour and National Service, at Bradford. It is the duty of such medical boards to examine men in the age groups 18 years to 25 years with regard to their physical and mental health in accordance with the Pulheems System and to classify them in one of four groups, defined as follows:

Grade I.—Those who have attained normal standards of health and strength and are capable of enduring the full amount of physical exertion appropriate to their age.

Grade II.—Those who are capable of undergoing considerable physical exertion not involving severe strain.

Grade III.—Those who present such marked physical disabilities or evidence of past disease as to render them not fit for the kind of service required by Grade II.

Grade IV.—Those who suffer from progressive organic disease and are for various other reasons permanently incapable of the kind of service required in any higher grade.

For the last few years men placed in Grades III and IV have been regarded as unfit for recruitment. In the years 1952 and 1953 the national average figure for men placed in Grades III and IV was 23.2%, a very surprisingly high number. In succeeding years this figure rose steadily and in 1957 27.8% were placed in Grades III and IV. Some areas exceeded this figure, notably Manchester, Liverpool, Birmingham, Nottingham, Dumfries (Scotland), Newcastle, Hull and Plymouth. Such findings caused great disquiet at the Ministry and special conferences of Chairmen of medical boards were convened to investigate these problems. Amongst the many conditions which caused men to be so graded, the most prominent were "poor physical development", ear diseases, respiratory diseases and

asthma, pulmonary tuberculosis detected by the preliminary X-ray of chest prior to the medical board, hernia, foot deformities, skin diseases, defects of vision, psychiatric states—i.e. emotional instability and mental dullness. Those men who appeared before the medical boards were only a small subsection of the community and with these disquieting findings we cannot by any stretch of imagination classify the standard of health of the community as being very satisfactory.

In the past the work of the general practitioner has been associated with the cure of disease and the relief of suffering and as a profession we are justly proud of our past achievements. In the future there is much work we can do in the field of preventive medicine to improve the standard of health of the community.

Housing.—In our everyday routine work, both in urban and rural areas, we have the opportunity of assessing the housing conditions of our patients whether satisfactory or otherwise. We can assess the degree of overcrowding, if it exists, and the insanitary or unhygienic home conditions which may be detrimental to the well-being of our patients. When patients suffering from pulmonary tuberculosis have returned home and there are no facilities for segregation we should forthwith get in touch with the Department of the Medical Officer of Health and recommend the desirability of arranging for alternative and more suitable accommodation. In Bradford we find the local health authorities are most considerate in acceding to the advice and requests of the family doctor.

In recent years we have all witnessed the gradual solution of the rehousing problem and the completion of new housing estates in every city and town throughout the country. In view of this we should not hesitate to support the claims of our patients, many of whom, especially in the urban areas, are still living in unsuitable conditions and who need more modern houses. We must not forget the housing conditions of the elderly, the geriatric cases, especially those who are suffering any physical deformity, arising for example from a crippling arthritis or a cerebral vascular lesion. Many of these find it physically impossible to climb stairs and in such cases we should put before the appropriate authority the relevant factors with a view to the provision of more suitable alternative accommodation. Many local authorities have made provision for such cases and have built bungalows with rooms all on one level and ideally suited for these crippled geriatric cases.

Control of infectious diseases.—Those of us who have been in practice since the middle 1920s are aware of the remarkable changes in the types of infectious diseases which have taken place since then. Diphtheria and scarlet fever during that period frequently appeared in epidemic form and carried a comparatively high mortality rate. Since the routine practice of mass immunization against diphtheria was introduced in 1940 notification of such cases has fallen from sixty thousand per year in the pre-war years to less than a hundred now with a very low death-rate. On the other hand, the incidence of the respiratory group of infectious diseases, measles and whooping-cough, has not decreased although there has been a decline in the death-rate of these two diseases due not only to the improvement in social conditions and improved nutrition of the children but very largely to the introduction of chemotherapeutic drugs and the antibiotics.

The system of dealing with infectious diseases by notification and isolation introduced in the last century and developed in the early decades of the present was designed partly to reduce the risk of infection amongst the contacts. This system still exists and the general practitioner, by early recognition and prompt notification of cases, can greatly assist the Medical Officer of Health and his department in controlling the spread of an epidemic. It is the duty of the general practitioner to ask for removal of such cases to hospital for isolation when they cannot be suitably isolated at home.

The family doctor should at all times explain to parents of children the necessity and urgency of having their infants immunized with the triple antigen now available for protection against diphtheria, whooping-cough and tetanus; also the importance of vaccination against smallpox which is nowadays so often overlooked. In recent months the family doctors in Bradford, as in other places, have been of considerable help to the local health authorities in the fight against poliomyelitis and the inoculations of children and young adults with the British or American vaccines.

A grave problem which is causing great concern to many general practitioners is the number of cases of dysentery which have been seen in increasing numbers in recent years. In the war years the number of cases of Sonne dysentery rose to epidemic prevalence and since 1945 has become endemic. Many of such cases are caused by contaminated food and the unclean handling of food and can be very serious when occurring in infants. Early diagnosis and isolation of the offending organisms should be

looked upon as a matter of great urgency. In the Bradford area, when such cases arise in our practice, notification to the Department of the Medical Officer of Health brings immediate assistance; the Department arranges for the collecting of specimens and the culture of stools for organisms which saves the time of the busy general practitioner. Also the identification and isolation of carriers is of the greatest importance in controlling the spread of the disease and we must impress on our patients and their families the strictest discipline as regards personal hygiene. Routine hand washing after the use of the toilet and before handling food would materially assist in controlling such infections. In the treatment of Sonne dysentery the newest antibiotic drugs have proved a great boon and should be administered regularly until cultures from the stools are negative.

The field of infectious diseases is a very suitable one for research by general practitioners. The great work in epidemiology done by Dr. William Pickles, late President of the College of General Practitioners, has received international recognition, especially his carefully collected observations on the spread of infective hepatitis occurring in his native Wensleydale. More recently, the "Report by a study group of the College of General Practitioners on the Complications of Measles" has received widespread and well-deserved credit from all branches of the profession. Surely these and other recently published results of research by members of the College prove beyond doubt that general practitioners can work together as a team and are ideally suited for carrying out research on the commoner diseases to which our patients are subject. The results of such research will in the future prove of benefit to the community.

Integration of the general practitioner with the School Medical Service.—In past years there has been a great gulf between the general practitioners on the one hand and the school medical officers on the other. There are many, even amongst Public Health Officers, who are of the opinion that the School Medical Service should be a general practitioner service, and I am very optimistic that in the future this will occur. With the approval of the Local Medical Committee the Medical Officer of Health for Bradford has recently introduced a very interesting pilot scheme which will probably be adopted later in other areas. This entails a closer liaison between the family doctor and the School Medical Service. For this experiment one area of the city was selected and a special clinic opened where all children who have reached the

school entrance age of 5 years are examined at a special session by the school medical officer and the child's family doctor. For each session 16 children are summoned who are on the list of one family doctor in that area. The child attends accompanied by his mother, and a full medical examination, including examination of the urine, is done conjointly by the general practitioner and the school medical officer. Also a simple intelligence test is given to the child. The general practitioner takes with him the medical record cards of the children so that the school authorities shall have a full record of the immunization and vaccination state of each child examined, also the past history of any medical or surgical conditions from which the child might have suffered. It is reported that already great benefits have accrued and I am informed that observers from the Ministry of Health and the Ministry of Education have been favourably impressed. A full report of this scheme will be published later. I might add that 90% of the family doctors approached to co-operate in this scheme accepted; they are remunerated for such services on a sessional basis.

Another scheme envisaged is the examination of boys and girls who have attained the school leaving age—an examination similar to the one conducted at the Medical Boards for National Service. What a great advantage such a scheme would prove to the Industrial Medical Officers! They would then have a complete Pulheems presented to them of the young men and girls on their entry into industry.

Ante-natal work.—With the discovery of Prontosil in 1934 and the research work of Sir Leonard Colebrook and his co-workers there was a startling drop in the maternal mortality rate and this rate has continued to fall as a result of the discovery of penicillin and also of improved ante-natal care. The majority of maternal deaths during the past few years have been due to toxæmia of pregnancy leading to eclampsia. Signs and symptoms of the toxæmic state arise during the course of pregnancy rather than in the post-partum period.

It is well recognized that many premature babies result from toxæmic states in the mother and that peri-natal mortality, i.e. stillbirths and deaths within the first week of birth, is closely related to prematurity.

All general practitioners practising midwifery realized the inadequacy of the ante-natal work laid down by the Ministry of Health when the National Health Service was introduced in 1948. A minimum of three or four ante-natal visits

and one post-natal visit was required to comply with the regulations for the payment of the midwifery fee. Two years ago "The Report of the Standing Maternity and Midwifery Advisory Committee of the Central Health Services Council" was published. Following its publication, representatives of the Local Medical Committee, medical representatives of the Hospital Services and representatives of the Local Health Authority, from the Bradford area, have met together on numerous occasions to discuss the implications and findings of this important document. Our local committee has formulated certain recommendations regarding improvements in ante-natal care which will raise the standard of ante-natal supervision, improve the hospital accommodation for cases of early toxæmia and, it is hoped, will thereby reduce the peri-natal mortality rate. It is advised that every case should be examined every two weeks up to the 24th week and subsequently every week. The main task of ante-natal care is to detect a sudden rise in blood pressure, a sudden onset of marked œdema, an increase of more than 2 lb. in weight during any one week, and the presence of albuminuria. If a general practitioner in the course of his ante-natal examination discovers any or all of the above signs, or such findings are reported to him by the midwife, the woman should be referred immediately for investigation in the ante-natal ward of the hospital.

Thus, by his very efficient ante-natal care, the general practitioner is one of the important members of the team working for the reduction of maternal mortality and peri-natal mortality.

Respiratory infections.—Chronic bronchitis is a disease which is more prevalent in the British Isles than in other countries. Certain localities show a greater incidence than others. In the West Riding of Yorkshire we see many cases of chronic bronchitis and in the winter months it is one of the commonest causes of incapacity from work with a corresponding loss to industry. A recent survey carried out at the Leeds Chest Clinic proved that the regular administration of broad-spectrum antibiotics during the winter months is of considerable benefit to such cases and the relapse rate is greatly reduced. Many sufferers from chronic bronchitis have been able to continue at work in spite of the heavy fogs, smoke pollution and humidity of the West Riding atmosphere during the winter months. Let us hope that in the future when atmospheric pollution is abolished by the creation of smokeless zones, we shall see a marked reduction in the incidence of chronic bronchitis in the industrial areas.

Upper respiratory infections of children, in past years, have been the cause of many cases of chronic suppurative otitis media with perforation of the ear drum and subsequent deafness. 16.5% of cases rejected by the National Service Medical Boards were due to ear diseases. During the past ten years it has been the routine practice of family doctors to treat cases of acute otitis media with antibiotics. This has produced marvellous results. Paracentesis and acute mastoid operations, so frequently performed previously, are seldom required at the present time as nearly all cases of acute otitis media resolve without perforation of the ear drum.

Other spheres in which the general practitioner can make his contribution to the improvement of the standard of health of the community lie in the field of psychological medicine and the early recognition of acute surgical emergencies.

It is clear that the work of the general practitioner has become more closely interlinked with the work of Medical Officers of Health. The rapid progress in the control of disease by powerful drugs, the prevention of certain diseases by immunization and the immense power of the State to improve conditions of life for the people have rendered this liaison inevitable. This close knitting together of general practitioners, Medical Officers of Health and Industrial Medical Officers constitutes a real advance in preventive medicine. But, however useful the general practitioner may be in this way, his essential sphere will always continue to be, so long as we are an independent profession and not mere servants of the State, in the homes of the people. He must use new methods of detection and treatment of disease, laboratory tests, investigations and radiological reports, but these methods must be his servants, not his masters. He must always bear in mind that behind every disease there is a patient and that his first aim is to cure and heal the sick. He will then take a place in their hearts that no specialist can win and as the trusted counsellor of his patients in time of trouble make his unique and splendid contribution to the health of the community.

Mr. R. F. Guymer (London):

The General Practitioner and the Industrial Medical Officer

I do not like the title "Industrial Medicine" as it is liable to convey the impression that it is a type of medicine that is quite different from ordinary medical practice. Nothing could be farther from the truth. Industrial medicine is the application of clinical knowledge to the problems that affect the health, happiness and

efficiency of the worker in industry. If we accept the definition of a factory as laid down in the Factories Act, there are over a quarter of a million factories in existence in this country. Only about 2% of these employ more than 250 workers. It will therefore be realized that in the large majority of cases there is no need for a full-time medical officer and consequently the work is, in many instances, done by a part-time medical officer who is often a general practitioner in the neighbourhood. However, it is important both from the humanitarian and economic aspect that everything should be done to maintain the health and happiness of the worker in his occupation and to guard him against the many hazards to health which he may meet at work. With regard to the small factories with few workers, such organizations as the Slough Industrial Health Service and the Harlow New Town Industrial Service are attempts to find a satisfactory solution to the problem of providing adequate health services to these small units.

A few years ago it was shown that in England and Wales the number of working days lost due to industrial disputes (i.e. strikes) compared to the number of days lost due to accidents and illness in industry was in the ratio of 1 to 280. This state of affairs may come as a surprise to many. A strike is news; the development of pneumoconiosis in a worker, whatever the cause, is not. Therefore it will be realized that not only is the treatment and, better still, the prevention of illness and accident in industry desirable for humanitarian reasons, but also on economic grounds.

The Industrial Medical Officer should, in my opinion, have had some experience of general practice: there is no better way to learn the joys and sorrows, hopes and fears that beset members of all ages of the population from time to time. He will give his opinion entirely on medical grounds and whether that opinion is what the employer or employee wishes to hear is not his concern. The doctor must never let his professional ethical conduct be affected by the exigencies of the moment or by the policy of the employer or of the trade unions. All medical records should be kept by the doctor in the medical department and these should not be shown to anyone other than the patient except with his written consent.

The pre-employment medical examination is very desirable before the employee commences work in a new job. I know that opinions vary about this. The examination should include a short questionnaire to be filled up by the applicant with regard to his previous illnesses. The examination is important because: (1) It

will reveal, in most cases, whether there is any physical or mental abnormality present. Such knowledge is important when deciding for what type of work the applicant is best fitted, quite apart from any technical training which he may have received. (2) It will avoid a claim being made for a disability said to have been caused by the employment, but which may have previously existed. For example a workman may claim that he has been "ruptured" due to having had to lift heavy weights. The rupture may have been present (without his being aware of it) before the commencement of his present employment and this can only be ascertained at the pre-employment medical examination. (3) The questionnaire should contain a question asking in what previous occupations the applicant has been engaged since leaving school. This is very important as some industrial diseases have a very long incubation period or a very considerable time may elapse before any symptoms or signs are revealed. (4) The Medical Officer may be able to ensure that an applicant will be given suitable work although physically handicapped, i.e. his handicap does not prevent the efficient performance of the job that he is allotted. Occupations such as car park attendant and lift attendant are specially reserved for disabled persons.

Details of the results of the pre-employment examination will not be revealed to the employer who will be informed only whether the applicant is fit or unfit for the job that it is intended he should do. Certain reservations or limitations with regard to the type of work that the applicant can perform should be stated if there is a possibility that an appropriate vacancy exists.

It is no part of the Industrial Medical Officer's duties to usurp the functions of the employee's general practitioner. Treatment in the medical department will be confined to dealing with emergencies and injuries which occur at work and the Medical Officer will not undertake consultations and treatment which come within the province of the general practitioner. In dealing with cases the Medical Officer will adopt one of three courses: (1) he may provide treatment at once, (2) he may arrange to admit the employee to hospital as an emergency, or (3) he will advise the employee to consult his family doctor.

In any case, except in very trivial matters, he will write to the general practitioner about his patient and will send the letter by post. By performing his duties honestly and giving his opinions without fear or favour the I.M.O. will gradually earn the trust and confidence of all with whom he comes into contact. From time to time employees will come to the Medical

Department requesting an interview with the doctor. When time allows, these requests should be granted as many a man or woman may be saved from a breakdown by some honest advice given in a kindly manner. Often the gratitude shown is out of all proportion to the doctor's assessment of the help that he has given. The M.O. can frequently make a valuable contribution to the maintenance of morale and personnel relations in the organization. But sentimentality must never be mistaken for kindness.

The rehabilitation of the injured workman is something in which team work may be important. The team should, when necessary and possible, include the I.M.O., the G.P., the Works Manager and, in many cases, the Shop Steward. No man or woman who is recovering from an illness should spend some weeks or months without any occupation if it can be avoided. In more than one industrial organization in this country the M.O. has been able to persuade the management to pay those workpeople who return after sickness absence the wage of their job before they were taken ill although the work to which they returned may not be the same as that which they undertook previously. An important part can be played by the G.P. in this question of rehabilitation by sending to the I.M.O. a short note concerning the reasons for the patient's sickness absence and stating what type of job, in the G.P.'s opinion, the patient is able to do. I would also stress the undesirability of issuing a medical certificate which states that a man or woman is now able to do light work. When one has spent some years as an industrial medical officer one realizes how very difficult it is, with all the goodwill in the world, for many organizations to provide so-called light work. What is extremely important and most useful is that the function of the patient should be accurately stated so that an attempt may be made to find him a job which is well within his physical and mental capabilities. For example, a man may have had a severe fracture of his leg which impairs his walking and yet the function of his hands and arms and the rest of his body may be unimpaired. It is in such cases that the Works Manager or Works Engineer may be able to adapt a machine so that it may be efficiently controlled by the disabled workman. Such care and trouble over organizing efficient rehabilitation is well worth while as it avoids the degeneration in morale which results from hanging about at home.

It is also helpful for both G.P.s and I.M.O.s to have knowledge of the provisions of the Disabled Persons (Employment) Act, 1944,

especially those sections dealing with Vocational Training and Industrial Rehabilitation Courses (Secs. 2 to 5).

If the Medical Department includes facilities for physiotherapy this may result in the injured person returning to work earlier than would otherwise be possible. Such treatment will be given with the knowledge, consent and collaboration of the G.P. concerned; in some instances absence from work may be completely avoided.

Application is sometimes made by an employee to retire from his work on medical grounds. Here the G.P. can be very helpful. He is the person who knows the home conditions of the workman and can, in many cases, help the I.M.O. in coming to a fair decision to all concerned with regard to the retirement of that employee.

The I.M.O. should in all appropriate cases consult with the G.P. either by telephone, letter or personal interview where necessary. He should always communicate with the G.P. when he wishes to visit an employee in his own home—this is the courtesy to be expected between professional men. The I.M.O. is always very pleased to welcome a G.P. at the place of work and to discuss his patient's condition and capabilities with him. I would like here to pay my personal tribute to the almost invariable help and kindness which I have received from other members of the profession with whom it has been necessary to communicate about employees.

Fisher (1953) has stated that . . . "no G.P. need be deterred from taking up industrial work by the fact that he has no formal training in preventive or occupational medicine". In some ways the G.P. is well qualified for such work. He knows the housing conditions in the neighbourhood and the means of transport available and he is probably familiar with the home conditions of certain workers on his list. It is hardly necessary to state that the G.P. who is acting as a part-time I.M.O. must strictly observe the ethical rules of conduct when seeing other practitioners' patients who are employees in the factory with which he is concerned.

Although the G.P. may have received no formal training in occupational medicine or control of environmental conditions it is now possible for him to take a course in these subjects on a part-time basis and it is desirable that he should do so if possible. Knowledge concerning such environmental conditions as heating, lighting, sound, sanitation, control of dust and food hygiene is very useful and necessary. It is frustrating to the doctor to carry out an inspection in a factory when he is

not sure for what conditions he should look, or the hazards which he is likely to find in any special process. I would stress that any doctor who takes up this work should make himself well acquainted with all the processes that are being used in the factory. Such information he may be able to obtain from the Works Manager, Engineer, and in some instances, the Works Chemist. When he has this information it is then possible for him to refer to one of several standard textbooks to see what may be the effects on the health of the workers in these different processes. It is important for him to remember that certain physical signs may be due to one of several causes. Tremor occurs, as we all know well, in conditions such as disseminated sclerosis and paralysis agitans. The occupational diseases, such as chronic mercurial poisoning, which cause tremor may not be so well known.

The health of the executive.—The most important single factor which affects adversely the health of the executive is, I am certain, the tempo at which he has to work. This has increased greatly over the last three decades due to the shortening of time and space by improvement in methods of communication and travel. A cable can be despatched to Australia in the morning and the answer may be on the executive's desk in the afternoon; he may attend a meeting in London in the early afternoon and be present at another meeting in New York early the next morning. O'Dwyer (1957) has dealt with this subject. Other adverse conditions, such as overeating and uncomfortable travelling to and from work, all take their toll of his mental and physical fitness. From experience I consider that there are four early cardinal signs of an impending breakdown: irritability, indecision, inability to delegate and the persistent taking home of work. This state of affairs may first be observed by the I.M.O. or by the G.P.; as Dr. George Beaumont has stated "many a patient who asks for a tonic really requires a sedative".

Whoever first observes these early signs, it is important that the one should communicate with the other in order that the appropriate measures may be taken to attempt to preserve the health of the executive and of any other worker who shows similar signs and symptoms (Sanders, 1958).

Industrial processes are always changing and methods of organization being revised. New toxic hazards are continually occurring; the use of radioactive substances is proceeding apace; automation is being adopted in an increasing

number of industries. The possible effects of automation on the health of workers are discussed by Welford (1958).

For further information see Guymer (1953).

REFERENCES

- FISHER, R. E. W. (1953) *Med. World, Lond.*, **78**, 176.
 GUYMER, R. F. (1953) *Med. World, Lond.*, **79**, 625.
 O'DWYER, J. J. (1957) *Hlth. Horiz.*, Winter No., p. 30.
 SANDERS, K. (1958) *J. Coll. gen. Practit.*, **1**, 381.
 WELFORD, A. T. (1958) *Brit. J. industr. Med.*, **15**, 99.

Dr. P. Lesley Bidstrup (London):

The General Practitioner and Research in Industrial Medicine

Research may be defined, very simply, as "diligent search" or "systematic investigation". The principles on which the practice of industrial medicine is based are those of general medicine applied to persons working in a particular environment, and the principles of research in industrial medicine are similar to those adopted by many famous clinicians. They are: careful observation, meticulous recording of the observed facts and finally diligent search or systematic investigation to explain them.

The enormous amount of time lost from work through sickness—over one million persons are absent for this reason at any one time—has already been mentioned. The illnesses giving rise to this are seldom rare or complex diseases of occupations, but the ordinary illnesses which every doctor is called upon to treat and to try to prevent. There may, however, be factors in the working environment which aggravate common conditions, and by knowing about these factors, the general practitioner is able to advise both patient and employer, to their mutual benefit. Inadequate ventilation, poor lighting, excessive noise, ineffective control of temperature and humidity, and the presence in the working atmosphere of excessive and possibly harmful dust, mist, fume or vapour are all conditions which can be altered, often by quite simple measures. Information about these factors and the exact nature of the work which a patient is called upon to perform can be obtained in two ways. The first is by careful enquiry into the patient's occupational history and the second by becoming familiar with the industries in the practice area.

Some general practitioners may feel that to add to their work careful observations about the occupations of their patients may be too arduous, but many a wrong diagnosis would be avoided if the doctor asking the standard question "What is your occupation?" had been taught

the importance not only of asking the question but of understanding exactly what his patient does and what jobs he has done since leaving school. The importance of the occupational case history and the procedure for eliciting it are described by Hunter (1955). The doctor who takes the opportunity, which is usually freely given by management, to make himself familiar with the industries in his area will find that he is able to assess more accurately the fitness of a patient for resuming his normal occupation and to discuss with the employer alternative work for patients who require this temporarily or permanently. Among examples of diseases not necessarily the direct result of occupation, but which may be aggravated by factors present in the working environment, I would like to mention bronchitis and emphysema. It is difficult to establish for these diseases a causal relationship with particular occupations, although it has been done for the chronic bronchitis and emphysema of cotton and flax operatives, and for the emphysema which is a feature of chronic cadmium poisoning. The patient who develops bronchitis is usually seen first by his general practitioner and, should his attacks recur, he is likely to be seen and treated in several or even many attacks before he is referred to a chest clinic or for other specialist advice. If the general practitioner enquires carefully on the first occasion about the patient's occupation, and particularly if he arranges to visit the factory where the man works, he will be able in many cases to make recommendations either to the man or to his employer—and often to both—which may result in fewer and less severe attacks of bronchitis in the individual patient. It may well be that there are occupations other than work with cotton, flax and similar dusts in which careful study initiated by general practitioners will reveal an unusually high incidence of chronic bronchitis and emphysema. Questions which the patient should be asked are whether or not there is dust present in the working atmosphere, and if so how it is produced. Does he know the nature of the dust? Is the dust an irritant, to him if not to his fellow workers, and are there other irritants such as mist or fume or vapour present constantly or intermittently? What ventilation is provided? Is this general ventilation or are there special ventilation arrangements, such as hoods and extraction fans, at certain points? Is he supplied with any form of dust mask or respirator? It is likely that in some cases where a diagnosis of bronchitis is made, particularly in a young man experiencing his first or second attack, a carefully elicited history including answers to the questions posed above would

suggest that chemical irritation might be responsible for the symptoms and physical signs. The X-ray will usually show no abnormality.

It may happen that the general practitioner has the opportunity to recognize a new industrial hazard because he has observed similar symptoms or signs in patients who are employed in the same factory. It is a simple matter to approach the management of the factory concerned and discuss the problem. Further investigation can then be arranged either in association with the company's own doctor or with the various bodies throughout the country who are prepared to undertake research into industrial medical problems. There are a number of organizations which the general practitioner may approach for advice and assistance. These include:

H.M. Senior Medical Inspector of Factories,
St. James's Square,
London, S.W.1.

The Department for Research in Industrial Medicine,
(Medical Research Council),
The London Hospital,
Whitechapel, London, E.1. (Dr. Donald Hunter)

The Occupational Health Department,
The London School of Hygiene and Tropical Medicine,
Keppel Street, London, W.C.1. (Dr. Richard Schilling)

The Occupational Hygiene Service,
Slough Industrial Health Service,
Farnham Road, Slough, Bucks.

The Industrial Medical Unit,
Central Middlesex Hospital,
Acton Lane, Park Royal, London, N.W.10. (Dr. T. O. Garland)

The Nuffield Department of Industrial Health,
University of Durham,
Durham. (Professor R. C. Browne)

The Nuffield Department of Occupational Health,
Victoria University of Manchester,
Manchester. (Professor R. E. Lane)

The Department of Social Medicine,
University of Oxford,
Oxford. (Dr. Alice M. Stewart)

The M.R.C. Toxicology Research Unit,
Woodmansterne Lane,
Carshalton Beeches, Surrey. (Dr. J. M. Barnes)

The Royal Institute of Public Health and Hygiene is planning to extend the scope of the work of its Laboratories at 23, Queen Square, London, W.C.1.

Much publicity has been given to proposals for the setting-up of occupational hygiene laboratories working on a regional basis and as part of a nation-wide industrial medical service. These developments are likely to be slow to mature, if only because of the lack of medical and scientific staff with the requisite training.

In a discussion during the 21st Anniversary celebrations of the Association of Industrial Medical Officers, on the need for occupational hygiene institutes sponsored jointly by interested government departments and industry, Dr. Charles L. Sutherland (1957) of the Pneumoconiosis Medical Panel, Bristol, reminded the meeting of two outstanding discoveries made in recent years in the field of industrial lung

diseases: the discovery by Dr. C. G. Shaver—a chest physician working near Niagara—of the effects on the lung of nascent aluminium and silicon driven off during the electrolytic preparation of aluminium abrasive; and the observation by Dr. A. Caplan in the course of routine work as a member of the Pneumoconiosis Panel in South Wales that progressive massive fibrosis of coal miners assumes a distinctive recognizable form when associated with rheumatoid arthritis. Dr. Sutherland further stressed that the careful work of individual Industrial Medical Officers may be the basis of the research of high-powered teams. I am sure that Dr. Sutherland would permit his remarks to be extended to include "the careful work of any doctor".

Not every doctor interested in industrial medicine has the good fortune to recognize for the first time a new disease or syndrome, however diligently he may search. What then can he expect to do which will contribute significantly to the prevention of disease caused or aggravated by occupation? The problem of chronic bronchitis has been mentioned as one which might well be best investigated, at least in the pilot stages, by general practitioners. Herford (1957) has indicated the requirements in the matter of the statutory examination of young persons. Meiklejohn (1959) reviews the development of industrial medicine in England and states the need to formulate a basic philosophy for its future development. He points out that factors such as excessive labour of children and young persons, undernutrition and malnutrition, grossly insanitary conditions, acute infectious diseases and physical strain had by 1957 been replaced by new problems requiring a new approach. These include the ageing population and the elderly workman, mental stress, the maintenance and promotion of health, and rehabilitation and resettlement of persons handicapped from any cause. I believe that general practitioners in liaison with Industrial Medical Officers and employers could contribute much to the solution of these problems.

REFERENCES

- HERFORD, M. E. M. (1957) *Youth at Work*. London.
 HUNTER, D. (1955) *The Diseases of Occupations*. London: p. 195.
 MEIKLEJOHN, A. (1959) *Brit. J. industr. Med.*, **16**, 1.
 SUTHERLAND, C. L. (1957) *Trans. Ass. industr. med. Offrs.*, **8**, 32.

Dr. R. J. F. H. Pinsent:

The General Practitioner in Industry

A part-time appointment in industrial medicine offers the general practitioner a unique opportunity to complete his observation of the

environment which surrounds his patients. Many large industries are still situated in large overcrowded cities where housing conditions are inadequate by modern standards. The words "industrial practice" conjure up a picture of dreary, dirty, red-brick streets with back-to-back houses, with open house drains in yards and closes and shared outside lavatories; the preservation of health is handicapped by such difficulties in maintenance of hygiene.

The counterpart to slum housing is the old-fashioned factory which now serves a purpose far removed from that for which it was designed and built. There may also be the added risk that processes now carried out in it may be dangerous in their own right. Even in this year of grace it is by no means unusual for a person to live in the type of house described and work in this kind of factory or works. To many the living and working environments are wholly at slum level.

For some there is a change, however, to the new housing estate where living conditions vastly improve; for others there is a curious paradox, for the works may be rebuilt to modern standards while the home remains a relic of the industrial revolution. It is in the modern factory, too, that industrial medicine begins to exert its influence, for these larger companies with insight and appreciation will establish an efficient medical service. Under such circumstances the working environment may, in terms of physical hygiene, be far ahead of the home. The home becomes the chief source of risk of disease and accident, for the vigilance of the Safety Committee and the M.O. eliminate predictable risks comparable to those of the unguarded fire, the fly-blown larder and the tubercle-spitting grandfather. From industrial practice the general practitioner may even learn something about preventive medicine in the home.

By its very contrast the emotional environment in which the worker finds himself in a modern factory may be adverse, rather than favourable, even under optimum physical conditions. He may be content in the comparative squalor of his home, and find it difficult to adjust to the standards expected of him by his employers, his workmates and his trade union. A large organization may become impersonal, and collective unrest, which seems to occur more in some industries than others, may be a manifestation of reaction to this.

Seeing the workers', and the employers', side of things from the viewpoint of the works doctor gives the general practitioner valuable insight into the management of his patients. If

the doctor knows what different jobs and trades involve in terms of physical or mental activity he can adjust return to work after illness or advise change with much greater authority. Further he may be able to identify emotional conflicts in the work context that show themselves as symptoms or overt illness in the home. Absence from work may be blamed on the wife, but often begins with the foreman.

In a rational system of health care no factory, however small, should be without a doctor to whom staff and works can turn for advice and guidance. In a small factory there is much good

housekeeping that can be initiated by a sound general practitioner even without special knowledge of technical processes. The Appointed Factory Doctor's responsibilities are limited, and he may not see beyond that which he is supposed to look for. In the same rational system no general practitioner in an industrial city should be without a professional interest in a small factory or two, situated conveniently in the practice area where one or two sessions a week will both enlarge and enrich his experience of practice, and his understanding of the "industrial patient" who is in his medical care and charge.

BOOKS RECENTLY PRESENTED AND PLACED IN THE SOCIETY'S LIBRARY

- American Academy of Pediatrics.** Report of Committee on the Control of Infectious Diseases. pp. 84. Evanston, Ill.: American Academy of Pediatrics. 1957.
- American Academy of Pediatrics.** Committee on the Fetus and Newborn. Resuscitation of the newborn infant. pp. 22. Evanston, Ill.: American Academy of Pediatrics. 1958.
- Bishop (W. J.).** A history of surgical dressings. pp. 90. Chesterfield: Robinson. 1959.
- Herman (E.).** Neurologdy polscy. pp. 462. Warsaw: Panstowowy Zaklad Wydawnictw Lekarskich. 1958.
- Cameron (V.), and Long (E. R.).** Tuberculosis medical research. National Tuberculosis Association, 1904-1955. pp. 325. New York: National Tuberculosis Association. 1959.
- Coltart (M.), Raine (H.), and Harrison (E.).** Social work in tuberculosis. pp. 144. London: Chest and Heart Association. 1959.
- Eaton Laboratories.** Nitrofurantoin bibliography. 1957. pp. 105. Norwich, N.Y.: Eaton Laboratories. 1957.
- Kettel (K.).** Peripheral facial palsy: pathology and surgery. pp. 341. Copenhagen: Munksgaard. 1959.
- Krayenbuehl (H.), and Yasargil (M. G.).** Die vaskulären Erkrankungen im Gebiet der Arteria Vertebralis und Arteria Basialis. pp. 170. Stuttgart: Thieme. 1957.
- McCarrison (Sir Robert).** Nutrition and national health. Being the Cantor Lectures for 1936. pp. 75. London: Faber. 1944.
- McMenemey (W. H.).** The life and times of Sir Charles Hastings, founder of the British Medical Association. pp. 516. Edinburgh and London: Livingstone. 50s. 1959.
- Malten (K. E.).** Beroepsekseem bij het verwerken van kunststoffen in het bijzonder van onverzadigde polyester harsen en aethoxyline harsen: een bedrijfsdermatologisch onderzoek. pp. 147. Leiden: H. E. Stenfort Kroese. 1956.
- Meshalkin (E. N.), and Smolnikov (V. P.).** Sovremennyye ingalyatsionny narkoz. (Contemporary inhalation anaesthesia). pp. 355. Moscow. 1959.
- Meyer-Steineg (T.), and Sudhoff (K.).** Geschichte der Medizin im Überblick mit Abbildungen. 4th ed. pp. 460. Jena: Fischer. 1950.
- Modell (W.).** The relief of symptoms. pp. 450. Philadelphia and London: Saunders. £2 16s. 1956.
- Modell (W.), ed.** Drugs of choice, 1958-59. pp. 931. St. Louis: C. V. Mosby. 1958.
- Odlum (D. M.).** Journey through adolescence. pp. 186. London: Delisle. 10s. 6d. 1957.
- Sarteschi (G.), and Bettolo (G. R.).** Il timo. pp. 401. Pisa: Omnia Medica. 1957.
- Society for General Microbiology.** Virus growth and variation. 9th Symposium of the Society for General Microbiology held at the Senate House, University of London, April 1959. pp. 272. Cambridge: Cambridge University Press. 35s. 1959.
- United States. Veterans Bureau.** Department of Medicine and Surgery. Medical research in the Veterans' Administration. 2 vols. Washington: Government Printing Office. 1959.
- University College Hospital.** The collected statistics of malignant disease seen at U.C.H., London, during the period 1946-1950. pp. 631. Shrewsbury: Wilding. 1958.

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Meeting
January 23, 1959

Hypophosphatasia with Congenital Dimples.—

S. D. V. WELLER, M.D., M.R.C.P.

S. B., male, born 9.6.58.

Dimples noted at birth over lower third of forearms and legs: these were remarkably symmetrical and varied from a shallow depression on forearms to deep pits over fibulæ, corresponding to exostoses. No bowing of long bones (Fig. 1).

Attended outpatients 8.9.58. No symptoms. Dimples unchanged. Sutures very wide. No other signs. Breast-fed.

Investigations.—X-rays: Skull: dense base; vault poorly ossified with wide sutures. Long bones: osteoporosis and irregularity at metaphyses, especially of humeri and tibiae (Fig. 2).

Blood picture normal. Calcium 11.7, phosphorus 4.1, cholesterol 185, sodium 340, potassium 21, urea 23 mg.%. Alkaline phosphatase 2 K.-A. units. W.R. negative.

Urine: Marked excess of phospho-ethanolamine.

Family history.—Elder brother healthy: alkaline phosphatase 10 K.-A. units: urine shows a little phospho-ethanolamine. Father well: urine normal but alkaline phosphatase 3 K.-A. units. Mother well: alkaline phosphatase 4 K.-A. units and urine shows a little phospho-ethanolamine.

Treatment.—Triamcinolone with penicillin cover from 31.10.58 to 29.12.58. Breast feeding maintained.

Progress.—No alteration in general appearance or condition.

1.11.58: Alkaline phosphatase 8 K.-A. units.

25.11.58: Bones markedly improved—almost normal (Fig. 3). Sutures closing and fontanelle rather tense.

10.12.58: Calcium 10.6, phosphorus 5.9 mg.%, alkaline phosphatase 6 K.-A. units. Urinary excretion of phospho-ethanolamine unaltered.

7.1.59: Bony improvement maintained.

20.1.59: Calcium 10.4, phosphorus 6.9 mg.%, alkaline phosphatase 6 K.-A. units.

Discussion.—Dimples have sometimes been recorded in cases of hypophosphatasia: such cases have all had bowed bones, but were not always severely affected. The frequency is such as to suggest the need for supervision till the diagnosis is excluded (bone structure may be normal at birth: Currarino *et al.*, 1957). Dimples without bowing have not been previously recorded in this condition.



FIG. 1.—Dimple over fibula.



FIG. 2.—Radiological appearances of forearm before treatment.



FIG. 3.—To show improvement after 8 weeks' steroid therapy.

Treatment with restricted calcium intake, no extra vitamin D and with triamcinolone was followed by a dramatic change in chemistry and X-ray appearances. This improvement is so far maintained (25.2.59), but the excretion of phospho-ethanolamine is little altered.

REFERENCE

CURRARINO, G., NEUHAUSER, E. B. D., REYERSBACH, G. C., and SOBEL, E. H. (1957) *Amer. J. Roentgenol.*, **78**, 392.

Diffuse Progressive Interstitial Fibrosis of Lungs in Infancy.—TREVOR P. MANN, M.D., M.R.C.P.

C. P., female. Admitted December 1953, aged 7 months, because of food refusal, failure to thrive, paroxysmal cough and vomiting. Died five weeks after admission and three months after onset of symptoms.

History.—First child. Birth weight 6 lb. 8 oz. Two months before admission coryza lasting two to three weeks. Simultaneously developed dry cough which slowly worsened; sometimes led to vomiting. No whoop. Motions green during first three weeks of illness. Course of Sulphatriad three weeks before admission.

Examination revealed wasting, pallor, cyanosis, respiratory distress and repetitive cough, not like pertussis. Afebrile. Slight injection throat and right tympanic membrane. Occasional added sounds over lungs. Liver normal in size. Admission chest X-ray: increased bronchial markings.

Immediate treatment.—Oxygen, intramuscular penicillin and tube feeding.

Clinical course.—Steady deterioration in spite of consecutive courses of penicillin, chlortetracycline, erythromycin and pre-terminally sulphadimidine together with streptomycin. Continuous oxygen required. Increasing pallor, cyanosis, dyspnoea and persisting dry irritative cough associated with progressive, diffuse, granular infiltration of lungs in serial radiographs. Body temperature normal except for a spike of 100° F. second day in hospital and range 98°–100° F. just before death. Pulse range 100–180 per minute; respiratory rate varied between 30–80 per minute. Terminally liver enlarged and neck veins became distended; no added sounds heard over lungs.

Investigations.—W.R. and Mantoux negative. E.S.R. (week before death) normal. ECG (four days before death) normal. No pathogens in repeated nose and throat swabs. Virus studies not done.

Autopsy.—The lungs in the gross were voluminous and firm to touch. The cut surface looked of the consistency of liver. Under slight magnification (Fig. 1) it was apparent that everywhere the normal lobular pattern was lost. Some parts were quite solid; other parts showed a distorted pattern of terminal air spaces. The latter were reduced in number, there being a great increase of connective tissue between them. The liver was enlarged and congested.

Histopathology.—The few air spaces which are visible are lined by cuboidal epithelium which shows a tendency to desquamate. In places they are formed into narrow tubules (Fig. 2). There is no pus formation, no specific inflammatory process and no evidence of pneumocystis infection. The abundant connective tissue is highly vascular (Fig. 3) with variable cellular infiltration, predominantly fibroblasts, lymphocytes and plasma cells but there are some polymorphs. This vascular connective tissue is rich in reticulin (Fig. 4); collagen is little in evidence.

Comment.—This case appears to fall into the group first described by Hamman and Rich (1944) under the title "acute diffuse fibrosis of the lungs", nowadays more correctly referred to as "diffuse progressive interstitial fibrosis of the lungs". In the last fifteen years some 60 or more cases have been published. So far only 3 accounts of the condition in childhood have been traced (Bradley, 1956; Baar and Braid, 1957; Feinerman and Harris, 1957). The last authors describe 2 cases, one of them an infant



FIG. 1.—Cut surface of lung under slight magnification showing reduction in number of terminal air spaces and great increase of connective tissue between them.

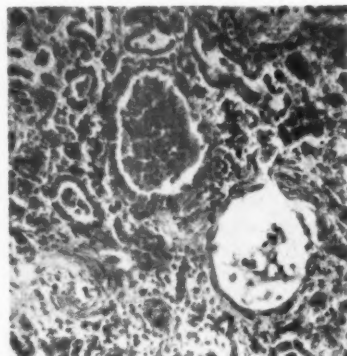


FIG. 2.—Lung. Sparse air spaces lined by cuboidal epithelium. In places (top right) they are formed into narrow tubules. H. and E. $\times 95$.

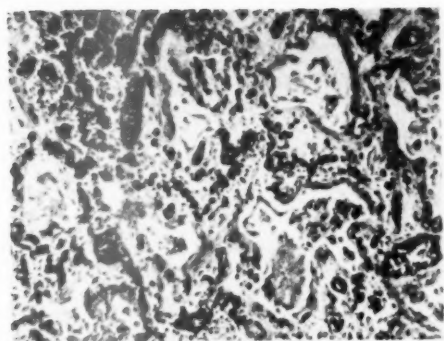


FIG. 3.—Lung. Demonstrates intense vascularity of the tissue. Mallory trichrome. $\times 95$.

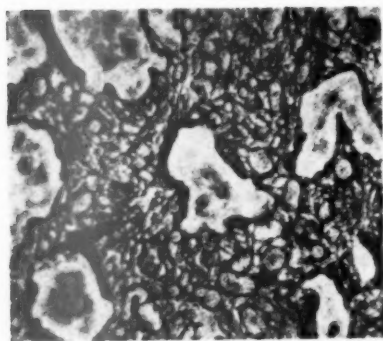


FIG. 4.—Lung. The vascular connective tissue is rich in reticulin. Paucity of air spaces is well shown. Numerous intervening smaller spaces represent blood vessels. Reticulin impregnation. $\times 95$.

whose age at the time of onset of symptoms coincides with that of the baby described here.

The clinical picture varies little from case to case and between age groups and is one of progressive suffocation with death either from respiratory insufficiency or pulmonary heart disease with terminal right-sided heart failure. There is, however, some variation between cases in the histopathological findings, probably depending on the age of the lesion. The dominant change in the lungs is a great increase of connective tissue between terminal air spaces. More often the fibrous proliferation is of a collagenous type; sometimes, as Golden and Bronk (1953) found, the connective tissue is, as in this baby, of stuff like granulation tissue, rich in reticulin and blood vessels.

The aetiology of this bizarre syndrome which affects subjects of all ages is obscure, but several causal hypotheses have been put forward. Tissue

hypersensitivity has been suggested by Peabody *et al.* (1950) and is supported by Read (1958). Recently Read and Holland (1959) have described an adult where the condition may have been precipitated by sulphonamides which is of interest as such preparations were used in the present case both before admission to hospital and just prior to death.

Diffuse interstitial fibrosis of the lungs is rare in childhood as the paucity of published cases shows. Five years have passed since this infant presented and a careful search has not revealed one further example of the condition in Brighton.

REFERENCES

- BAAR, H. S., and BRAID, F. (1957) *Arch. Dis. Childh.*, **32**, 199.
 BRADLEY, C. A. (1956) *J. Pediat.*, **48**, 442.
 FEINERMAN, B., and HARRIS, L. E. (1957) *Proc. Mayo Clin.*, **32**, 637.
 GOLDEN, A., and BRONK, T. T. (1953) *Arch. intern. Med.*, **92**, 606.
 HAMMAN, L., and RICH, A. R. (1944) *Bull. Johns Hopk. Hosp.*, **74**, 177.
 PEABODY, J. W., PEABODY, J. W., Jr., HAYES, E. W., and HAYES, E. W., Jr. (1950) *Dis. Chest.*, **18**, 330.
 READ, J., (1958) *Amer. Rev. Tuberc.*, **78**, 353.
 —, and HOLLAND, R. A. B., (1959) *Thorax*, **14**, 71.

Myasthenia Gravis.—ELIZABETH BEATTIE, M.B. (for CHARLES PINCKNEY, F.R.C.P.).

I. S., female. Born 26.7.46. Aged 12 years.

History.—May 1958: Complaining of inability to move legs and falling approximately twice daily. Thinks she has blackouts at these times. Symptoms persisted till admission in October 1958. Three weeks before this she developed weakness of her arms and was unable to brush her hair. Also diplopia on one occasion. Tended to sit with eyes half-closed. Weakness worst after climbing stairs, walking or cycling. Onset of attacks preceded by giddiness. No headache, vomiting, dysphagia or dysarthria.

No relevant previous or family history.

On admission 16.10.58.—No physical abnormality.

Progress.—28.10.58: Suddenly developed weakness of arms, intention tremor of arms, and nystagmus to left. Legs normal. Speech and swallowing normal. Reflexes brisk and equal. Plantars flexor. Fundi normal. During next three weeks also developed weakness of orbicularis oris, erector spinæ, glutei and flexor muscles of leg. Nystagmus disappeared.

Investigations.—Full blood count, blood urea, serum electrolytes, glucose tolerance curve, C.S.F., X-ray skull, spine and chest: all within normal limits. No enlarged thymus. EEG slightly abnormal; changes are non-specific.

At this stage diagnosis rested between familial

periodic paralysis, myasthenia gravis and muscular dystrophy.

Prostigmin test.—0.75 mg. Prostigmin subcutaneously produced normal muscle power within ten minutes.

Treatment.—75 mg. pyridostigmine in twenty-four hours in 5 divided doses has given her completely normal power.

Comment.—Myasthenia gravis is a very rare disease in childhood. Thanks to the Prostigmin test the diagnosis is now much simpler and the incidence has therefore apparently increased. In spite of this, Osserman (1958) in a review of the literature on juvenile myasthenia gravis could find only 190 cases. It is more common in girls than in boys.

The most common presenting symptom seems to be ptosis which is bilateral, although one eye may be affected more than another. Diplopia is not a common feature, as in adults, although it may be present transiently. When the skeletal muscles become affected the weakness is remarkably symmetrical as we found in our case where she was unable to lift her arms above her head. The cranial nerves are also affected and the disease may present as acute respiratory distress precipitated by some infection. The response to an injection of Prostigmin is dramatic and life-saving.

REFERENCE

OSSERMAN, K. E. (1958) *Myasthenia Gravis*. New York and London.

Transient Neonatal Myasthenia.—R. W. SMITHELLS, M.R.C.P., M.R.C.P.Ed. (for P. R. EVANS, M.D., F.R.C.P.).

Baby G., male, aged 10 weeks (born 10.11.58).

History.—Mrs. G. (born 1925) developed symptoms of myasthenia gravis in 1945. The following year her thymus was removed by Sir Geoffrey Keynes. She takes Prostigmin (about 200 mg. daily) and ephedrine, and needs an occasional Prostigmin injection.

Her first baby was a girl born in 1955. She was a 36-weeks premature weighing 4 lb. 13 oz. delivered by the breech. She was rather limp and had to be tube fed for three weeks. The second baby was born in November 1958 six weeks before term and weighed 5 lb. Forceps were used because of delay in the second stage of labour. He cried well at birth. A few hours later he was noticed to be lethargic and there was an excessive amount of mucus in the pharynx. The following morning he was completely limp, there was much mucus and he easily became cyanosed. He made no attempt to suck a bottle and the cry became very weak.

A diagnosis of neonatal myasthenia was made

and Prostigmin 0.25 mg. was given intramuscularly. There was a dramatic response within five minutes, the baby becoming more active and crying more strongly. Prostigmin was repeated every three hours at first and then less frequently, being discontinued on the thirteenth day.

For a week the baby showed poor muscle tone, cyanotic attacks after most feeds, oral and nasal regurgitation and a feeble cry. At 2 weeks cyanotic attacks stopped and muscle tone improved. At 3 weeks regurgitation had stopped and all feeds were taken by spoon. At 4 weeks all feeds were taken from a bottle and the baby showed normal activity. He has remained well. Prophylactic tetracycline was given for three and a half weeks.

Comment.—Myasthenia gravis occurs in two forms in childhood. The adult form of the disease may appear at any age and a few children have been reported in whom symptoms dated from birth. This condition has been called congenital or juvenile myasthenia. Occasionally more than one member of a family is affected. The other form is transient neonatal myasthenia in which the symptoms are self-limited. These infants are invariably the offspring of myasthenic mothers. It has been estimated (Teng and Osserman, 1956) that about 15% of babies born to myasthenic mothers show transient neonatal weakness.

Symptoms are sometimes recorded as being present from birth but more characteristically they are noted when the child is a few hours old or even as late as the third day. The common features are an expressionless face, feeble cry, generalized hypotonia, weak or absent sucking reflex, excessive amounts of mucus and a tendency to cyanotic attacks. The average duration of symptoms is three weeks, varying from about ten days to six weeks. A few deaths have been reported: with one exception (Kibrick, 1954, Case III), these have been in the first week of life.

The diagnosis of transient neonatal myasthenia can be made by the dramatic response to Prostigmin or Tensilon.

(A film was shown illustrating the response to Prostigmin.)

The most important aspect of the management of these babies is continuous observation. They do not swallow well and are full of mucus. They regurgitate feeds through mouth and nose and easily become obstructed. Prophylactic chemotherapy is probably wise. Prostigmin cannot shorten the duration of the illness but by improving swallowing it may help to tide the baby over the dangerous first week.

The main interest of this condition is its mechanism which is unknown. Many myasthenic mothers have had normal babies before

having affected ones but there is no record of a normal baby after a myasthenic one. There are many records of two consecutive myasthenic babies. A suggested explanation is the placental transmission of some curare-like substance. This seems improbable since the onset of symptoms is usually delayed for several hours after birth and foetal movements are usually normal throughout pregnancy.

An alternative explanation is that symptoms are due to Prostigmin withdrawal. The diagnosis of neonatal myasthenia has never yet been proved in the offspring of an untreated mother. It is interesting to note that although myasthenia gravis in children was described in the nineteenth century, neonatal myasthenia was not recognized until 1942 (Strickroot *et al.*) a few years after the general introduction of Prostigmin treatment. It seems possible that the unborn infant's muscles become adapted to function normally in the presence of Prostigmin. The baby would be born with a supply of Prostigmin and symptoms would only appear when this became exhausted.

I should like to thank Mr. T. L. T. Lewis for permission to show this baby.

REFERENCES

- KIBRICK, S. (1954) *Pediatrics*, Springfield, **14**, 365.
 STRICKROOT, F. L., SCHAEFFER, R. L., and BERGO, H. L. (1942) *J. Amer. med. Ass.*, **120**, 1207.
 TENG, P., and OSSERMAN, K. E. (1956) *J. Mt. Sinai Hosp.*, **23**, 711.
- Cold Antibody Type Virus Pneumonia.**—D. H. GARROW, M.R.C.P. (for CHARLES PINCKNEY, F.R.C.P.).
 R. B., girl, aged 9 years 11 months.
History.—Onset of cough 14.10.58. During the first week of her illness a diagnosis of the cold antibody type of virus pneumonia was suggested by a troublesome cough, widespread coarse bubbling rales in the chest, failure to respond to penicillin and a normal white blood count.
 On 24.10.58 her father, and on 13.11.58 her mother, developed a similar illness.
 The diagnosis was supported by the results of serial rapid tests for the presence of increased cold agglutinins.
 The child's tests were negative in the first week, positive in the second, and negative again by the third week. Her father was not tested until the second week of his illness when his test was strongly positive. Her mother's illness was less severe and tests for increased cold agglutinins were negative in both the second and third weeks.
Comment.—The family were shown to emphasize the value of taking a family history and investigating parents in the case of any child with pneumonia and to illustrate the

practical value of the rapid test for an increase in cold agglutinins (Garrow, 1958). The regular use of this test over the past five years has shown that the incidence of cold antibody type virus pneumonia has fluctuated markedly.

The distribution of 136 children diagnosed during this period at the Victoria Hospital for Children, London, is shown in Table I.

TABLE I

| | 1954 | 1955 | 1956 | 1957 | 1958 |
|--|------|------|------|------|------|
| Children with cold antibody type virus pneumonia | 39 | 24 | 15 | 9 | 49 |
| Families with more than one member affected | 9 | 3 | 0 | 1 | 7 |

The increased incidence in 1958 occurred in the second half of the year.

REFERENCE

- GARROW, D. H. (1958) *Brit. med. J.*, **ii**, 206.

Congenital Siderocytic Hypochromic Aplastic Anæmia.

—H. B. HILTON, M.B. (for J. L. EMERY, M.D., and J. LORBER, M.D.).

A girl aged 25 months of pure English ancestry who presented at the age of 11 weeks with a minor respiratory infection was found to have a severe hypochromic anæmia which proved refractory to oral and parenteral iron therapy.

The erythrocytes showed marked hypochromia, anisocytosis and poikilocytosis (Fig. 1), and an

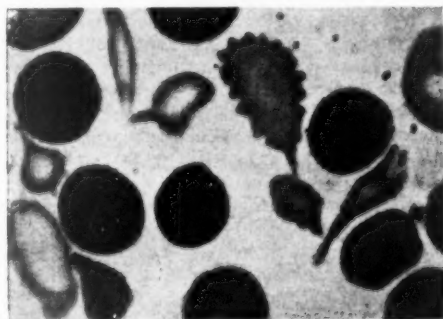


FIG. 1.—Peripheral blood after transfusion showing the contrast between normal donor cells and the patient's bizarre shaped hypochromic cells. ($\times 1,300$.)

occasional siderocyte was present in the peripheral blood (M.C.V. 64.5 c. μ , M.C.H. 19.6 $\gamma\gamma$, M.C.H.C. 25%). Leucocytes and platelets were normal in number and morphology. Reticulocytes always below 1%. Red cell fragility was slightly decreased.

The bone-marrow was relatively hypoplastic. The normoblasts showed deficient haemoglobin production and at the same time a great increase in the number of iron-staining granules. Many erythrocytes contained similar large coarse

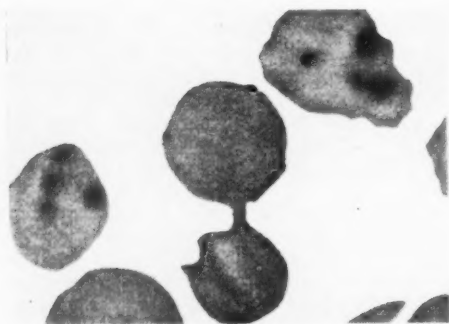


Fig. 2.—Siderocytes in bone-marrow. Two erythrocytes contain large coarse granules which stained positively for iron. ($\times 2,050$.)

granules, giving a positive staining reaction for iron (siderocytes) (Fig. 2).

Serum iron $205 \mu\text{g./100 ml.}$ (normal $100 \mu\text{g./100 ml.}$), serum unsaturated iron binding capacity $70 \mu\text{g./100 ml.}$, total iron binding capacity $275 \mu\text{g./100 ml.}$ Direct Coombs test negative. Serum bilirubin less than 0.5 mg./100 ml. on numerous occasions. No abnormal haemoglobin was detected by electrophoresis or chromatography. Urinary excretion of porphyrins was not increased. Hepatic and renal function tests were normal.

Investigation of the patient's parents and only sibling revealed no haematological abnormality.

There was no physical or mental retardation, and no evidence of chronic infection, neoplastic process, acute or chronic blood loss, or osteopetrosis. The only physical sign was pallor and the only symptom lassitude when particularly anæmic.

The following drugs have been given: Oral iron (ferrous sulphate) $270 \text{ mg.} \times 28$, intramuscular iron (Imferon) $1 \text{ c.c.} \times 12$, copper sulphate $1 \text{ mg.} \times 28$, ascorbic acid $500 \text{ mg.} \times 21$, thyroid $60 \text{ mg.} \times 56$, cyanocobalamin $175 \text{ mg.} \times 42$, cortisone $150 \text{ mg.} \times 28$, pyridoxine $50 \text{ mg.} \times 7$, crude liver extract (Plexan) $2 \text{ c.c.} \times 4$. No treatment given produced haematological response either by rise in the reticulocyte count or haemoglobin level.

Blood transfusion is necessary to maintain life, five blood transfusions having been given since birth. After transfusion the haemoglobin falls at the rate of approximately 1 gram\% per week until the level of approximately 4 grams\% is reached, when symptoms necessitate transfusion.

Discussion.—The presence of gross hypochromic anæmia in the presence of adequate body stores of iron is suggestive of a thalassæmia-like syndrome. The absence of increased

haemolysis, detectable abnormal haemoglobin, family history, hepatomegaly, splenomegaly, and bone lesions is against this diagnosis. The anæmia appears to be due to a congenital metabolic error of haemoglobin synthesis, and it is possible that later studies may reveal a specific enzyme defect.

Acute Infantile Gaucher's Disease.—R. H. R.

WHITE, M.R.C.P., D.C.H. (for Professor ALAN MONCRIEFF, C.B.E., M.D., F.R.C.P.).

P. C., female, aged 8 months, born 25.5.58, seventh child.

History.—Normal delivery at 42 weeks, after pregnancy uncomplicated except by small antepartum hæmorrhage at 38 weeks. Birth weight $7 \text{ lb. } 5 \text{ oz. (3.3 kg.)}$. Sucked well; breast fed. Normal until 3 months, after which motor development ceased, feeding became difficult and weight gain diminished. Became intermittently rigid; no fits. Mother said she was "like the other child who died".

Family history.—Parents healthy, unrelated. Four surviving siblings healthy. First child died of congenital heart disease.

Sixth child, female, born 10.10.56. Difficult labour, cord twice round neck. Attacks of opisthotonos, from birth. Admitted Great Ormond Street at 5 months, diagnosed "? Cerebral palsy due to birth hypoxia"; hepatosplenomegaly unexplained. Died at home aged 6 months. No autopsy.

On examination.—Gross opisthotonos, increased muscle tone in all limbs, symmetrically increased tendon reflexes. Fontanelle tense. Intermittent laryngeal stridor. Spleen 5 cm. below costal margin, liver 3 cm. ; both felt firm.

Investigations.—No subdural effusions, C.S.F. and ventriculogram normal. EEG: Mild abnormality with diminished activity anteriorly. Slight amino-aciduria "suggestive of liver dysfunction". Liver function tests normal. Serum cholesterol 187 mg.\% . Bone-marrow normal. Splenic needle biopsy reported by Dr. Martin Bodian to show "considerable infiltration with typical Gaucher cells giving a positive PAS reaction".

Treatment and progress.—Prednisolone 15 mg. per day. No change in condition or in hepatosplenomegaly after three weeks. Developed bilateral aspiration pneumonia and died on 29.12.58 in spite of treatment with tetracycline.

Autopsy confirmed Gaucher's disease, the liver, spleen and bone-marrow being diffusely infiltrated. Bilateral lower lobe aspiration pneumonia was the immediate cause of death. Details of the neuropathology of this case are to be reported elsewhere.

Discussion.—Owing to the gross opisthotonos this infant's hepatosplenomegaly was missed on admission and the tense fontanelle and spasticity at first suggested the possibility of an expanding intracranial lesion. The subsequent finding of splenomegaly and recollection of the older sister's illness led to the suggestion that both siblings might, in fact, be cases of acute infantile Gaucher's disease. In retrospect, these cases reflect the characteristic clinical features of this disease—opisthotonos, muscular rigidity, mental retardation, laryngeal spasm and splenomegaly—which have been well described by Moncrieff (1930), van Crefeld (1953) and others. Predominantly neurological, they are presumably related to diffuse degenerative changes with positive periodic acid-Schiff staining reaction, found in the neurons, in addition to gliosis and perivascular cellular infiltration of the brain (Norman *et al.*, 1956). The presence of Gaucher cells in the brain is rare (Barlow, 1957).

A review of the records of the Hospital for Sick Children, Great Ormond Street, from 1918 to 1958 inclusive, has revealed 14 histologically proven cases of Gaucher's disease, of which 5 were of the acute infantile variety. Inclusion of the sister of the present case brings the total number of acute cases to 6 in forty-one years. There were 3 boys and 3 girls. The main clinical features are summarized in Table I and the ages

TABLE I.—CLINICAL FINDINGS IN 6 CASES OF ACUTE INFANTILE GAUCHER'S DISEASE

| | | | | | | |
|-------------------------------------|----|----|----|----|----|---|
| Feeding difficulty .. | .. | .. | .. | .. | .. | 5 |
| Mental retardation .. | .. | .. | .. | .. | .. | 6 |
| Head retraction and opisthotonos .. | .. | .. | .. | .. | .. | 4 |
| Spasticity .. | .. | .. | .. | .. | .. | 5 |
| Splenomegaly .. | .. | .. | .. | .. | .. | 6 |

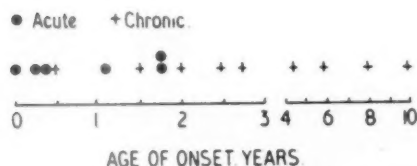


FIG. 1.—Age of onset in acute and chronic Gaucher's disease.

of onset of the acute and chronic cases are shown in Fig. 1. Although 3 of the chronic cases developed symptoms under the age of 2 years the clinical picture was quite distinctive; abdominal swelling due to splenomegaly was the presenting symptom, while neurological signs were absent.

In the present case the diagnosis was established by splenic biopsy, obtained by a Gilman's liver biopsy needle, inserted under general anaesthesia with controlled apnoea. Bone-marrow smears

failed to show Gaucher cells in spite of the subsequent autopsy findings. Geddes and Moore (1953) reported a case of infantile Gaucher's disease with normal bone-marrow smears and a diagnostic splenic biopsy. A review of the biopsy findings, obtained from the Great Ormond Street records (Table II), suggests that spleen or liver

TABLE II.—BIOPSY FINDINGS IN ACUTE AND CHRONIC GAUCHER'S DISEASE

| Biopsy material | Acute | | Chronic | |
|-----------------|--------------|----------|--------------|----------|
| | No. obtained | Positive | No. obtained | Positive |
| Bone marrow .. | 3 | 1 | 4 | 2 |
| Spleen .. | 2 | 2 | 8* | 8 |
| Liver .. | 1 | 1 | 5 | 5 |

*Splenectomies.

biopsy affords a greater chance of making a firm diagnosis than does a bone-marrow puncture. This is perhaps explained by Dr. Bodian's finding, in another acute case previously examined at autopsy, that the bone-marrow infiltration was focal whereas that in the liver and spleen was diffuse. According to Bruton *et al.* (1955), needle biopsy of the liver in infancy is safe in skilled hands, and this is probably true of spleen biopsy, although both procedures would be contraindicated in those cases of chronic Gaucher's disease in whom there is a bleeding tendency due to thrombocytopenia.

There is no known treatment for the acute disease and the prognosis is grave. The 6 cases in this series died between the ages of 5 months and 3 years.

REFERENCES

- BARLOW, C. F. (1957) *J. Neuropath.*, **16**, 238.
 BRUTON, O. C., METZGER, J. F., and SPRINZ, H. (1955) *Pediatrics*, Springfield, **16**, 836.
 CREFELD, S. VAN (1953) *Advanc. Pediat.*, **6**, 192.
 GEDDES, A. K., and MOORE, S. (1953) *J. Pediat.*, **43**, 61.
 MONCRIEFF, A. A. (1930) *Arch. Dis. Childh.*, **5**, 265.
 NORMAN, R. M., URICH, H., and LLOYD, O. C. (1956) *J. Path. Bact.*, **72**, 121.

Endocardial Fibroelastosis in One of 3-Year-Old Twins—Review Six Years Later.—J. J. KEMPTON, M.D., M.R.C.P.

J. M. was shown to the Section of Paediatrics six years ago (Kempton, 1953). There had been repeated severe episodes of cardiac failure for which she was first admitted to hospital at the age of 3 months and which ceased in her fourth year. Failure always seemed to be precipitated by respiratory infection and the response to digoxin was generally good. Her sister, I. M., showed no symptoms or signs of heart disease.

Detailed investigation of blood groups (Dr. S. Lawler, Galton Laboratory, University College) and examination of finger and thumb



FIG. 1A.—J. M.



FIG. 1B.—I. M.

Heart shadows showing some difference in shape of cardiac outline.

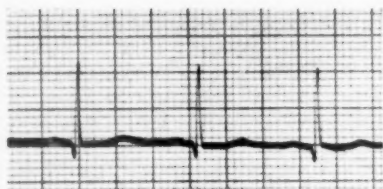


FIG. 2A.—J. M.

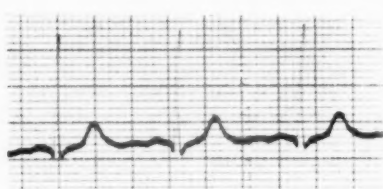


FIG. 2B.—I. M.

Left ventricular leads showing flattening of T waves in tracing of affected twin.

prints carried out in the Police Laboratory gave strong evidence that the twins are uniovular.

There were no murmurs. Limb pulses and blood pressures were normal. X-ray showed an enlarged globular cardiac outline. No abnormality of rhythm was detected in many ECG tracings. A conduction defect noted in one was thought to be due to digitalis and in general the only change noted was flattening of T waves in the left ventricular leads.

Now at the age of 9 years she is the equal in physical activity of her twin sister and they are closely alike in build and appearance. She is living a normal life with no restrictions.

There is still a difference in heart outline (Fig. 1) and in ECG (Fig. 2).

Comment.—It seems that the original diagnosis may have been correct. The long course of the illness makes the alternative diagnosis of "isolated" or "idiopathic" myocarditis less likely, though it cannot be excluded.

It has become apparent in recent years (Bonham-Carter, 1954) that endocardial fibro-elastosis occurring as part of the pattern of congenital heart disease is not, as had been thought, an almost invariably fatal cause of early failure and a few cases have been recently described in young adults (Guraieb and Rigdon, 1956).

REFERENCES

- BONHAM-CARTER, R. E. (1954) In: *Recent Advances in Pediatrics*. Edited by D. Gairdner. London: p. 389.
 GURAIIB, S. R., and RIGDON, R. H. (1956) *Amer. Heart J.*, **52**, 138.
 KEMPTON, J. J. (1953) *Proc. R. Soc. Med.*, **46**, 271.

The following cases were also shown:

Two Cases of Congenital Hypoplastic Thrombocytopenia with Limb Deformities.—Dr. A. J. G. SHEPHERD (for Dr. CHARLES PINCKNEY and Dr. J. L. STAFFORD).



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Q. What are the main advantages of using 'Saluric' as well as 'Inversine'?

A. 'Saluric' potentiates the *hypotensive* action of 'Inversine' and allows a smaller *effective* dosage of 'Inversine' to be used, with a consequent reduction in ganglion blockade side-effects.

Q. What is the best method of administering these drugs?

A. By commencing with 'Saluric' (dosage range 0.5—1.5 G. daily) and adding 'Inversine' (2.5 mg. twice daily initially).

Q. What if the patient is *already receiving* 'Inversine'?

A. *Immediately* 'Saluric' is administered, the existing dosage of 'Inversine' is reduced by 25 to 50 per cent, and re-adjusted later according to the patient's response.

Q. Can 'Saluric' be used with other hypotensive agents?

A. 'Saluric' can be used concurrently with other ganglion blocking agents (e.g. hexamethonium, pentolinium and pempidine) as well as with rauwolfia derivatives and hydralazine.

'SALURIC'• (Chlorothiazide): Supplied as 0.5 G. tablets.

'INVERSINE'• (Mecamylamine hydrochloride): Supplied as 2.5 mg. and 10 mg. tablets.

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Section of the History of Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS,
Bt., C.B., M.A., D.M., F.R.C.P.

Meeting
March 4, 1959

Richard Caton (1842–1926) Pioneer Electrophysiologist

By The Rt. Hon. Lord COHEN OF BIRKENHEAD,
M.D., D.Sc., LL.D., F.R.C.P., F.S.A.

Liverpool

RICHARD CATON was one of Liverpool's most distinguished citizens, and when he died in 1926, at the age of 84, the medical profession lost one of its great men.

He graduated from Edinburgh in 1867, and three years later became M.D. and received the gold medal for his thesis on the "Migration of Leucocytes". A year after graduation he settled in Liverpool (he belonged to a Lancashire family originating in Heysham and Caton) and soon became associated with the Liverpool Royal Infirmary School of Medicine as physician to the hospital and lecturer in physiology. He played an important role in the development of that Medical School into the University College

of Liverpool, and he was from 1882 to 1891 the first holder of the Chair of Physiology, a post which he combined with that of physician at the Royal Infirmary. It was at that time customary in most medical schools for chairs in anatomy and physiology to be part-time, and held by a surgeon and physician respectively. Caton had long recognised that such joint appointments were unjust and injurious to the preclinical sciences. Within a few years of his arrival in Liverpool, when he was, at the age of 31, Lecturer in Physiology at the Royal Infirmary Medical School, he delivered the introductory annual address on "Physiology in Relation to the Health of the Community and the Advance of Medicine", which reveals an enviable prescience. He pleaded for Government support for medical research in phrases with a singularly modern ring:

"The time will doubtless come when our Government will recognise the importance of aiding this department of science. When we consider the scores of thousands of pounds expended on scientific experiments for the perfecting of weapons, for the discovery of the best mode of defence and attack in warfare, to say nothing of the millions spent in carrying out such results, the ultimate object of which, of course, is the defence and preservation of national life and property; when we consider the vast sums thus spent, it would not appear unreasonable to expend a few thousands, a mere fraction in comparison, in aid of the investigation of other modes of saving life—life which is in much greater actual peril in another way. There are other foes besides military invaders."

Sir Charles Sherrington and Sir Henry Dale have both recalled how in their early days distinguished physicians poured scorn on physiological experiment as an aid to the interpretation of the phenomena of disease. Yet here in 1873 is Caton's exhortation:

"Let me recommend you to pay attention to each department of study; don't undervalue parts which at present may seem to you to possess no

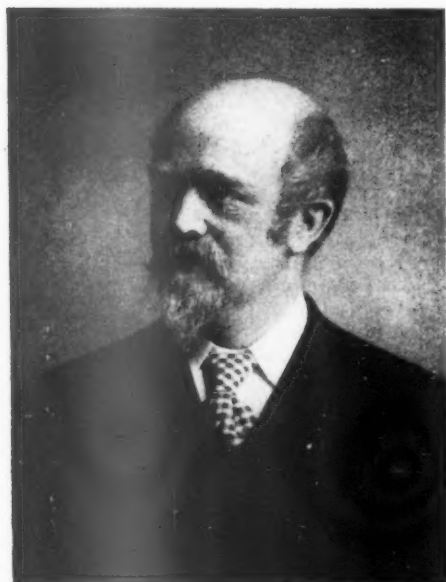


FIG. 1.—Richard Caton.

immediate utility in Medical practice, such as branches of chemistry or practical physiology. You will subsequently find how valuable they are. Scientific knowledge is becoming more and more important to the Medical man. During the period in which you will be practising your profession, Medicine will advance rapidly. If we could look forward twenty years hence, we should probably find that some astonishing strides had been made. Let me, then, strongly urge upon you, while giving a due attention to practical Medicine and Surgery, to take care that you acquire a sufficiently sound basis of scientific knowledge to be able to keep pace with the advances of your profession."

And one final quotation from this address which embodies his plea for a full-time chair of physiology:

"The work of investigation, as I have said, is difficult, laborious, and often expensive. At present it is carried on mainly by medical practitioners, who earn their bread by the practice of their profession, and who gain little or nothing by their scientific work, except the esteem of the few who are able to understand and estimate it. The public in general know nothing about these subjects. The science is thus at a disadvantage, depending too much on the efforts of isolated men who can only spare to it a small part of their time. The gain to the science, and the ultimate benefit to the country, would probably be great if one or more Government-supported laboratories were established, and some of the more eminent physiologists paid to devote their entire time to the work."

By 1891, he had persuaded George Holt, a member of a family of Liverpool ship owners, whose name is identified with many of Liverpool's philanthropic enterprises, to endow a full-time chair in the University College. Its first incumbent was Francis Gotch, who left four years later to become the first Waynfleet Professor of Physiology in the University of Oxford. He was succeeded by Sherrington who held the George Holt Chair for eighteen years, during which many of his classical contributions to the physiology of the nervous system were made.

Caton's interest in the University he did so much to establish never waned. He reached the high office of Pro-Chancellor, and was its first representative on the General Medical Council, and held that office until he died in 1926.

He became a city councillor and devoted much time to the promotion of higher standards of public health. In 1907, to the gratification of all, he was chosen Lord Mayor of the city. He was a classicist and historian. He travelled extensively in the eastern Mediterranean countries, and published papers on "The Temples and Ritual of Asklepios, Hippocrates and Cos", and "The Medicine and Medicine God of the

Egyptians." He served on the council of the Royal College of Physicians and delivered the Harveian Oration. During the First World War he was honorary Colonel, West Lancashire Division, R.A.M.C., and was tireless in his efforts to secure the comfort and nursing of the sick. He was in so many good causes a selfless and indefatigable worker, and contributed felicitously to so many humane studies, that of him a modern Johnson might well repeat—"Nullum quod tegerit non onnavit."

Yet none of his obituary notices recalled what will be his strongest claim to scientific fame, namely, that he was the first to demonstrate the presence of electrical currents in the brain. Indeed this work might well have remained buried were it not that Hans Berger in his classical paper of 1929, "Über das Elektrenkephalogramm des Menschen" (*Arch. Psychiat. Nervenkr.*, **87**, 527), writes:

"Caton had already (1874) published experiments on the brains of dogs and apes in which bare unipolar electrodes were placed either on the surface of both hemispheres or one electrode on the cerebral cortex and the other on the surface of the skull. The currents were measured by a sensitive galvanometer. There were found distinct variations in current, which increased during sleep and with the onset of death strengthened, and after death became weaker and then completely disappeared. Caton could show that strong current variations resulted in brain from light shone into the eyes, and he speaks already of the conjecture that under the circumstances these cortical currents could be applied to localization within the cortex of the brain."

The references which Berger gives to Caton's work are three: *Brit. med. J.* (1875) ii, 278; *Zbl. Physiol.* (1890) **4**, Nr. 25, p. 785; Bechterew, V. M. (1902) *Die Energie des lebenden Organismus*. Wiesbaden; p. 102.

Caton's work which resulted in the earlier reference of 1875 appears to have been inspired by a communication of David Ferrier to the Royal Society in 1874 (*Proc. roy. Soc.*, **22**, 229) on the "Localization of Function in the Brain" in which he recorded the effects of ablation by cautery and of electrical stimulation of the cerebral cortex, in order to test "the theory of Hughlings Jackson, that localized and unilateral epilepsies are caused by irritation or 'discharging lesions' of the grey matter of the hemispheres in the region of the corpus striatum".

Ferrier mapped out those areas of the cerebral cortex which gave focal movement on faradic stimulation of the cortex and noted how these corresponded to the sites of paralysis which followed ablation of specific areas of the cortex. This paper was communicated to the Royal

Society by Dr. J. Burdon Sanderson, and was to be followed by two others, both entitled "Experiments on the Brain of Monkeys"—the first on April 29, 1875 (*Proc. roy. Soc.*, **23**, 409), and the second as the Croonian Lecture on May 13, 1875 (*Proc. roy. Soc.*, **23**, 431).

It was Ferrier's 1874 paper which led Caton to reflect that electrical currents might be detected in the brain even at rest. He applied successfully to the British Medical Association for a grant towards the expenses of his proposed investigation. By the spring of 1875 he had obtained interesting results, and a letter from Burdon Sanderson (undated but post-marked May 5, 1875) shows that Caton wrote to Burdon Sanderson who had sponsored Ferrier's papers, and who was then a Vice-President of the Royal Society, to enquire if it would be proper, since the grant for the work came from the B.M.A., to communicate his findings to the Royal Society. Burdon Sanderson answered:

49, Queen Anne Street, W.

Dear Dr. Caton,

I have not been so prompt as I should have liked to have been in reply to your letter.

Unquestionably there can be no objection to your making a preliminary announcement to the Royal Society as to the results of your experiments. It would not, however, be a bad plan to give Mr. Hart for the Journal [Hart was editor of the *British Medical Journal*] a note at the time the paper is read to the effect following: 'On Thursday evening a note was communicated to the R.S. by Dr. Caton embodying certain very important results, etc., etc. Our readers are aware that Dr. Caton received a grant, etc., etc.'

This would I think be gratifying to the Association and would be quite unobjectionable. It might come out the day after the reading of the paper.

I am very glad that you have got such important results. Theoretically the subject is a very difficult one and wants many additional observation(s) to bring it into clearness.

Yours truly,

(Sgd.) J. B. SANDERSON.

On the flap of the envelope was a PS.—"Ferrier's new experiments are to be read next meeting, May 13."

Through the kindness of the Royal Society's librarian, Mr. I. Kaye, I have been able to search through the *Proceedings* and record books of the Society, but have failed to find any reference to Caton's having followed up his suggestion. Indeed, the first reference to his work in this field is recorded in the *British Medical Journal* (1875, ii, 278) where there appears a summary of a communication he made to the Annual Meeting of the B.M.A. in Edinburgh, in July 1875, when the Section of

Physiology was meeting under the Presidency of Burdon Sanderson. This is the reference which Berger gives. It reads:

"*The Electric Currents of the Brain*. By Richard Caton, M.D., Liverpool.—After a brief *résumé* of previous investigations, the author gave an account of his own experiments on the brains of the rabbit and the monkey. The following is a brief summary of the principal results. In every brain hitherto examined, the galvanometer has indicated the existence of electric currents. The external surface of the grey matter is usually positive in relation to the surface of a section through it. Feeble currents of varying direction pass through the multiplier when the electrodes are placed on two points of the external surface, or one electrode on the grey matter, and one on the surface of the skull. The electric currents of the grey matter appear to have a relation to its function. When any part of the grey matter is in a state of functional activity, its electric current usually exhibits negative variation. For example, on the areas shown by Dr. Ferrier to be related to rotation of the head and to mastication, negative variation of the current was observed to occur whenever those two acts respectively were performed. Impressions through the senses were found to influence the currents of certain areas; e.g., the currents of that part of the rabbit's brain which Dr. Ferrier has shown to be related to movements of the eyelids, were found to be markedly influenced by stimulation of the opposite retina by light."

Caton published no further details of his experiments until 1887, when he read a paper entitled "Researches on Electrical Phenomena of Cerebral Grey Matter" to the Ninth International Medical Congress at Washington, D.C., U.S.A. (*IX Int. Congr. Med.*, **3**, 246). This H. R. Viets uncovered in 1950.

In purpose and concept this paper shows how far ahead Caton was of his time. He was well acquainted with the electrical phenomena of peripheral nerves which DuBois-Reymond and Donders, amongst others, had investigated, but he could find only two references to electrical changes normally occurring in the brain. The first, published before his earlier communication, was DuBois-Reymond's paper on "The Electrical Current of the Frog's Brain"; the second was by James Dewar and J. G. M'Kendrick on "Experiments on the Effect of Light, in which a portion of the Brain was included in the circuit" (*Trans. roy. Soc. Edinb.*, 1876, **27**, 160). DuBois-Reymond's experiments recorded for the central nervous system what was well established in other tissues, viz. that an injured area is electrically negative to an intact area. The experiments of Dewar and M'Kendrick showed that light entering the eye causes electrical changes in the brain. They carried out experiments on both

frog and pigeon and summarized the results of these:

- "1. *The frog*.—On bisecting the head of a newly killed frog with a sharp pair of scissors, it is possible to obtain a longitudinal section of the brain, with the various parts in their natural position, then to carefully cut away the anterior and posterior portions of the brain, leaving only the middle portion in contact with the optic nerve. On placing this preparation between the clay points, so that the one touches the surface of the cornea, while the other is in contact with the brain substance, a strong deflection is obtained which is sensitive to light, and follows the course observed in the case of the frog.
- "2. *The pigeon*.—The effect was also traced into the optic lobes of a living pigeon (deeply under chloroform), the head of which was securely held between the clay points of the electrodes. The optic lobes in the pigeon are easily exposed. The following were the effects of this observation:—*a*, When one pole was applied to the left optic lobe, and the other to the cornea of the right eye, a deflection was obtained which was sensitive to light; *b*, when the pole was removed from the right eye, and applied to the cornea of the left, a smaller deflection was obtained, also sensitive to light; and, *c*, when light was allowed to impinge on both eyes, while the one pole was in contact with either eye, and the other with the left optic lobe, the result was nearly double that produced by the impact of light on one eye alone, either right or left. These effects may be explained by the decussation of the optic nerves in the optic commissure."

Dewar and McKendrick demonstrated in effect that light shone into an eye gives rise to electrical currents which flow in brain tissue along recognizable paths.

Caton's earlier experiments and those reported in 1887 were of a different nature. They were designed to answer two questions: "1. Does the grey matter of the brain give evidence of electrical currents comparable with those of nerve fibre and muscle? (2) If such currents exist are they related to the functions of the brain, and will the study of such currents throw any light on those functions?" To answer these questions he used cats, rabbits and monkeys. He ingeniously applied small, light, non-polarizable electrodes with fine clay points to any region of the exposed brain which he sought to examine, and connected these electrodes by light insulated wires suspended from a support overhead to a reflecting galvanometer. The animal experimented on was tethered loosely to the centre of a table a yard square, and allowed to move about, eat and drink, at its pleasure. Many experiments failed from technical difficulties, but he was

able to record currents from the surface of the brain which fluctuated, for example, with body movement or anaesthesia. But his observations of Ferrier's earlier described motor and sensory areas are of greatest interest and are best recorded in his own words:

- "1. There is a region in the grey matter of the rabbit's brain, stimulation of which by the interrupted current causes rotation of the head to the opposite side. In the brain of the monkey there is also a corresponding centre. In several instances I found that by producing a sound, or by offering food on the one side of the animal experimented on, I could induce it to turn its head voluntarily to that side; when this movement was made, electrodes placed on the centre in question of the opposite hemisphere showed a fall in the current toward zero, in fact a negative variation; the movement of the needle exactly coincided with the movement of the animal's head to the opposite side. Probably the explanation is that the brain cells of the region were in a state of functional activity connected in some way with the head movement, and that a negative variation of the electric current occurred similar to that which is well known to occur in a nerve fibre when a reverse impulse traverses it.
- "2. It is difficult to induce a rabbit or a monkey to perform any definite voluntary act and to repeat the action frequently enough for the basing upon it of a physiological inference. The act of mastication is more easily induced than any other. A rabbit will frequently eat a piece of fresh lettuce, and a monkey will usually eat a raisin or a piece of raw potato as soon as it is offered him. I experimented, therefore, frequently on that centre of the brain which when stimulated causes masticatory movements. In half the animals used, I found that when the non-polarizable electrodes were placed on this centre, negative variations occurred invariably when the animal masticated, the variations lasting as long as mastication and ceasing when mastication ceased. In some instances it was evident that the thought or expectation of food caused the movement of the needle. If I showed the monkey the raisin but did not give it, a slight negative variation in the current occurred. When the electrodes were applied to this region, I found that sensory impressions made on the mouth or face caused a similar movement of the needle; for example, the introduction of the handle of a scalpel into the mouth, pinching of lips or cheeks, or stimulation of skin of face by interrupted currents. It seemed from this experiment as though the centres for movement of jaw, for perception of sensory impressions from mouth and face, and for ideas of food derived through the eye, coincided or were closely adjacent to one another.

The area associated with these functions appeared to be small. I frequently had to search for it for some time. If the electrodes were not upon it but merely near it, no relation was observed between mastication and the movements of the galvanometer.

- "3. Placing the non-polarizable electrodes on a given motor area, for example, Ferrier's region No. 1, related to the hind limb, I found that if I stimulated the limb with an interrupted electric current, negative variations frequently, though not always, occurred. Stimulation of other parts of the body had no such effect. This experiment seemed to indicate that the centres for the production of muscular movement and for sensory perception in the skin coincided for the limb in question.
- "4. Not unfrequently after continuous exposure of a hemisphere of the brain, spasms occurred in one or both limbs on the opposite side. If I placed the non-polarizable electrode on the brain area corresponding to the movement, I usually found that a strong negative variation coincided with each spasm. This was seen in numerous experiments, though not invariably.
- "5. I found no part of the brain the electrical currents of which were influenced by stimulation by odors or by sound.
- "6. I tried the effect of alternate intervals of light and darkness on seven rabbits and four monkeys, placing the electrodes on the region (13) stimulation of which causes movement of eyes. In three rabbits and two monkeys I found that light caused negative variation almost invariably. In those five experiments in which I was successful the relation between the intervals of light and darkness and the movements of the galvanometer needle was quite beyond question. If I partially shaded the animal's eye from the light, the effect on the electric current was diminished. The exact way in which the light produced its effect is not so easy to determine. It may have excited the visual centre especially, or it may have acted as a general excitant to the whole brain, or the result may possibly have been due to the heat radiated from the flame acting on the electrodes; I think one of the first two theories is more probable than the third."

In brief, Caton showed that electrodes applied to the brain manifested electrical currents which increased during the suspension of functional activity. These electrical currents were modified by activity of the cortex being almost invariably diminished when the cortical area examined was functionally active. He regarded the electrical change demonstrated in Ferrier's areas which accompanied the motor or sensory activity associated by Ferrier with these areas, as further presumptive proof of cerebral localization. There is in these observations clear anticipation

of the later observations of Berger, Adrian, Penfield and others.

It is difficult to evaluate Caton's work with precision in the absence of exact data relating to the sensitivity of his galvanometer (he describes it as Sir William Thomson's reflecting galvanometer) and of the temporal shape of the observed changes in current. Emeritus Professor H. A. Ormerod, his son-in-law, tells me that all Caton's manuscripts, records and instruments relating to his physiological work were destroyed several years ago. There is the natural danger of reading into the experiments more than the technical shortcomings would justify, but none can doubt that they were most advanced in conception for their time, especially the attempt to observe these electrical changes in the cortex of an animal—mobile and active. Some have ascribed the findings to injury potentials similar to those described by DuBois-Reymond in peripheral nerves, but this cannot be the explanation of the influence on the magnitude of deflection of such factors as functional activity of the cortex, and anaesthesia, and the act of dying. There are, however, certain difficulties to explain. For example, it is difficult to see how a motor discharge and an afferent stimulus could produce deflections of the same polarity: if the cortical surface on discharge becomes negative in relation to a distant point, it should become positive when an afferent impulse is travelling upwards, as indeed was found by Adrian and others. Further it seems unlikely that the mere sight of food would be sufficient to produce currents from the sensorimotor area for the face. The same criticism may be applied to the localization of the visual centre in area (13), the area controlling the movements of the eyes.

Not the least interesting offshoot of this work is that Caton became involved in a claim for priority. This is worth relating because it adds to our knowledge of the development of electrocorticography, and illustrates vividly a somewhat discreditable feature of the science of that period. On November 8, 1890, there appeared in the *Zentralblatt für Physiologie* (4, 473), a paper by Dr. A. Beck, Assistant in Physiology in the University of Cracow, on "The ascertainment of the localization of the functions of the brain and spinal cord by the electrical manifestations." He sought "to prove in a direct way that by stimulation of a centripetal nerve the centres of this nerve come into action". He made two sets of experiments, the first on the spinal cord of frogs; the second, and these are relevant, examined the currents of the cerebral cortex in warm blooded animals. In dogs and rabbits, he sought for the cortical centres of vision, touch, and hearing. He and Caton used similar elec-

trodes (those of DuBois-Reymond) but his galvanometer was Hermann's, compensated by rheochord to measure power and observe direction of current flow. He describes his experiments thus and I would stress especially that part of his description which appears to anticipate Berger's α -rhythm:

"I denuded one hemisphere of the surrounding soft parts and bones, being careful not to damage the dura mater before the total denuding of the hemisphere. After this the dura mater was carefully split and turned over on the edges of the bone which were blunted and smoothed as much as possible. On two points of the cerebral cortex I placed the non-polarizing electrodes. Already at the first experiment I noticed—and this was constantly repeated—that the range of movement after the connecting of the electrodes to any two points of the cerebral cortex of the hemispheres was not a steady one; the fluctuations were not synchronous with the rhythm of respiration nor with the pulse, nor were they dependent on any movements of the animal since they appeared also in curarized dogs. Therefore, neither the pulsations of the brain nor changes in the cortical vessels nor voluntary movements can be considered as the cause of these oscillations. They were entirely independent and stopped during stimulation of centripetal nerves as well as under a deep chloroform narcosis.

"I feel, therefore, entitled to consider these oscillations as the expression of continuous changes which take place in the condition of the action of the cortical centres. This activity can be suppressed by the stimulation of a certain group of centripetal nerves and was entirely stopped by the narcosis.

"On stimulation of the eye by magnesium light an electro-negative tension arose in the occipital lobe of the opposite hemisphere of the brain. A strict limitation of the area of vision was found in the dog while in the rabbit they were scattered all over the posterior part of the hemisphere, which fact agrees with the results of the experiments of Munk.

"The manifestations were not so distinct on stimulating the sense of hearing by sound as by stimulation of the eye. The reason for this may have been that the connexion of the electrodes immediately to the lower surface of the temporal lobe caused great difficulty. However, I found on stimulating the nerve of the skin that the current derived from the corresponding part of the cerebral cortex showed distinct changes which gave some indication as to the origin as to the condition of action."

This was followed in the next issue of the *Zentralblatt* (4, 537) by a letter which indicates a practice not uncommon, especially on the Continent in those days, namely, attempting to secure priority by depositing a letter embodying preliminary findings, usually incomplete and unsubstantiated, on any scientific problem. This letter was from the Professor of Physiology in the University of Vienna, the celebrated Ernst Fleischl von Marxov. It read:

"The contents of the original paper of Dr. Beck prompts me to publish a sealed letter which was deposited with the Imperial Academy of Sciences in Nov. 1883, and which was opened and read at the last meeting of the class for mathematics and natural science by my request.

"The letter which was so opened had literally, without any addition or omission, the following text:

'Vienna, 6 November, 1883.

In the course of this year, I have made a series of experiments on different animals, the results of which appear to me important enough to secure for myself priority concerning these findings by the deposition of this letter with the Imperial Academy.

'If one connects two symmetrically lined points of the surface of the cerebral hemispheres to a sensitive galvanometer by non-polarizing electrodes one will not find any or only a very little movement. If one stimulates an organ of sense the central projection of which is one of those points connected with the galvanometer, one will get a movement in a certain direction; if one stimulates the corresponding organ of sense of the other side, one gets a movement in the opposite direction. The experiment for instance succeeds very beautifully by connecting the points which have been defined as the centre for the perception of sight by Munk on both sides and by alternately exposing the one or the other eye to light.

'If one leaves the electrodes on the places just mentioned and stimulates the animal by vapour of ammonia which one allows to act on nasal mucosa, or if one pinches the extremity of an animal, or one burns it with a hot needle, one gets none or extremely weak movements, obviously caused by spread of current. One is, however, able easily to find those points of the cerebral cortex by this method where strong disturbances of the electric equilibrium are caused by the stimulation in question so that one can use this fact as a method to find those parts of the cerebral cortex where certain sensory stimuli are transmitted to our consciousness.

'If you chloroform an animal in which these experiments have succeeded and repeat the experiments during the narcosis of the animal, one does not get even the trace of a reaction in the galvanometer. If one allows the animal to wake up and repeats the experiments again one gets positive results again. From this follows, firstly, a confirmation of the conclusions drawn from the experiments generally, and secondly, that the narcosis by chloroform (and ether) is really due to temporary paralysis of the cerebral cortex, and not as some people believe to an interruption of the memory.

"These experiments succeeded not only by direct connexion with the denuded cerebral cortex, but also by connexion with the corresponding points of the dura mater, even with the bones of the skull deprived of the periosteum. One has to be careful in these experiments that the cortex does not cool, for this also causes paralysis. It will perhaps even be possible to perceive the currents arising by different psychic acts of one's own brain by connecting the skin of the head."

Professor Marxov's communication continues:

"On the contents of this seven-year-old letter, priority is claimed.

"Into the differences in a few details of our observations I am not disposed to enter because I will presently find an occasion for critical comment on the communication of Dr. Beck, or for a detailed comparison of the worth of the two observations.

"But I must briefly point out one circumstance, that in the results of my investigations the answer is contained to the question which hitherto has remained unsolved, i.e. whether narcosis brings about an interruption of the faculty of memory or a temporary annihilation of perception? Finally, it is perhaps superfluous to stress that in spite of the authorization of my claim to priority, the merit of Dr. Beck's investigations remains undisturbed, for he could have had no knowledge even of the existence, let alone of the content of my sealed communication to the Imperial Academy of Sciences in Vienna."

This letter from Professor Marxov stimulated a pertinent reply from Dr. Beck (*Zbl. Physiol.*, 1890, 4, 572). He wrote:

"Nature held and still holds innumerable problems in its secret. But it is no difference to science if the solution of one of these puzzles remains under the seal of nature itself or under that of the Imperial Academy of Sciences in Vienna. The priority of the discovery, therefore, is due to the one in my opinion who has broken the seal of nature of a secret without bringing it under another one.

"Besides the struggle for the priority in this case appears to me at least unnecessary. This is not a discovery but the application of an already known method to the solution of new questions."

Beck then tells how he had been led to his research by the examination question set for a prize which he gained. The question was: "It has to be stated if one is able to demonstrate the condition of action of the nerve centres by so-called negative movement, and in the case of positive results to demonstrate by negative movement: the localization of the reflex centres for the lower extremities in the spinal cord, the centres of vision of the cerebral cortex and the automatic centres in the medulla oblongata."

Beck then refers to earlier research in the electrophysiology of the nervous system by DuBois-Reymond, Hermann and Siczewow, but gracefully concludes: "Lastly let me say how pleased I am that my results have been so rapidly confirmed by so admirable a scholar as Professor Marxov."

Following this Caton wrote to the editor a letter published on March 14, 1891 (*Zbl. Physiol.*, 4, 785) in which he refers to the priority claims of Marxov and Beck for the discovery of electrical currents in the cerebral cortex. He continues:

"In 1874, the B.M.A. awarded me a grant to investigate the electrical changes in the cerebral

grey matter. In 1875, I made a report to the physiological Section of the B.M.A.

Then follows the full text given above of the report of the paper in the *British Medical Journal* (1875, ii, 278). After referring to his Washington paper in 1887, he concludes:

"It is not my purpose to belittle the fame of the learned physiologists, still I did make these discoveries myself, and as I mentioned above, have published them, so I think it will be admitted that I was already the earlier discoverer."

This closed one episode in the life of a man who held that physiology was the basis of sound medical practice, and applied the scientific method to his problems, at a time when empiricism held undue sway. He sought a rational basis for his therapy. For example, in rheumatic fever he asked himself the pertinent question—"Joints recover: why does the endocardium fail to do so?" And the answer came, "The rheumatic joint rests, but not the rheumatic heart", and so he instituted complete rest for months. He contributed to the explanation of the effects of counter-irritation by showing that stimulation of the skin of the chest, thermal, electrical, mechanical or chemical, produced changes in the calibre of the arterioles of the lung, also that similar stimulation modified the electrical potential of the intestinal wall, as shown by the galvanometer. These observations led him to try the effect of small blisters over the third, fourth, fifth and sixth intercostal spaces in acute rheumatic heart disease, long known as Caton's blisters. He read widely and was quick to apply the knowledge so gained. Within a few months of Pierre Marie's recording that acromegaly is associated with pituitary tumour, he had induced F. T. Paul to operate on a patient afflicted with the disease.

But above all Caton stressed the whole man, and it was his yearning for human betterment that motivated him in all his work—whether in treating a patient, in campaigning for slum clearance, for secondary and University education, for a great new Cathedral, or for the many other causes dear to him.

I recall but one short chapter of his life and contribution to medicine here, not from a feeling of parochial pride, though I am indeed proud to belong to a Medical School of which he was one of the most luminous figures, but also to pay a somewhat belated tribute to one who made a notable and perspicacious contribution to physiology, and who saw what was hidden from many of his contemporaries, the signal part which physiology was destined to play in the development of the science of medicine.

Meeting
April 1, 1959

Medical Education in the Tudor Period

W. S. C. COPEMAN, O.B.E., F.R.C.P.

London

THE Tudor background was one of change; change from the careless extrovert sunlit world of the Middle Ages with its comparative prosperity, security and stability, an ordered hierarchy of men on earth and saints in heaven, to a turbulent, doubting, self-conscious new society where nothing was stable or secure any more. The discovery of the New World had introduced monetary inflation and unemployment, and even the landscape was changing as hedges and ditches began to mark the enclosures for the new and profitable sheep-farming which was replacing the open arable fields of the earlier age.

Great domestic buildings of exotic type were springing up, and the sumptuous Court of King Henry VIII was filled with the wit and learning of the new-style Renaissance courtiers and savants. Surrey, Wyatt, Linacre, Erasmus, More and Fisher were all there; music and painting were in fashion, and the romantic theme-song which sounds in our ear is of love and spring and hunting, and of rediscovery of the secrets of the golden past. All this culminated in the glories of the Elizabethan age. But the undertones were of melancholy. The expectation of life for a man of this period was not more than forty years, and there was of necessity a spartan attitude towards pain, plague and cruelty, whilst bitter religious persecution was at its height only just across the Channel.

At the outset of the Tudor period there was no profession of medicine, and consequently all practitioners were "free-lances". The physician was a learned scholastic whose M.D. was the product of fourteen years of deep and largely sterile study; he had very little practical acquaintance with the diseases he purported to treat. The apothecary was an unincorporated pharmacist, who also supplied largely the needs of the lowlier members of the populace for day-to-day doctoring and who would often present to the physician the case history and the urine of his more difficult patients for diagnosis and direction. Then there was the barber whose prescriptive right was all minor surgery and tooth-drawing; major surgery would be referred to one of the members of the Guild or Fraternity of Master Surgeons who were the élite consultants of those times. More numerous than the sum of all these categories, however, were the "mighty army

of quacks and Empiricks, those scum of our populace" who being largely itinerant were readily available and were very prosperous.

Medicine in those days, and indeed until living memory, was, in the absence of basic scientific knowledge, predominantly an art. This was based upon the teaching of Hippocrates the Greek, as codified by his follower Galen nearly six hundred years later. After the break-up of the Roman Empire all this knowledge passed to the Arabs who preserved it throughout the Dark Ages and reintroduced it, although by now in debased form, when they conquered Southern Europe in the twelfth century. This was the corpus of mediaeval European medicine, which by decree of the Church could not be doubted—only explained. All further knowledge and experience was grafted on to this old stock so that no real progress could be made until Harvey in the seventeenth century was able to refound medicine upon a new basis.

Let us remember, however, that, in spite of all this, medicine did eventually become the mother of scientific method, and so of all modern sciences. Her daughters have long ago outstripped her, but Walshe has bidden us not to forget that the Faculty of Medicine was awarded great prestige and esteem on this account in Tudor times and for the several centuries following.

Medical teaching and the curriculum.—Medical education at this time was not of a very formal type but was carried out at the universities by means of lectures and disputations on the texts of the old Masters. The general belief that medicine and science owe no significant debt to university teaching prior to the Renaissance, however, cannot be conceded. The medical student of the Tudor period, whilst spending seven years taking his M.A. before being allowed to proceed to study in the Faculty of Medicine, was being trained through the seven liberal arts in the power of orderly thought and its expression in terms of general principles. The resultant intellectual system was, and still is, an essential for scientific thought. What it continued to lack throughout most of the Tudor period was the additional conception of the experimental method of observation and its corollary of inductive reasoning, but this was to be added to

their intellectual armamentarium within a few years. The Medical Faculty, by excluding from its lecture halls all who worked in any way with their hands, kept alive the purely intellectual tradition and prevented its debasement to a technical craft, which is what happened in the case of surgery; but this also postponed the introduction of clinical bedside teaching until the seventeenth and eighteenth centuries.

This apparently undue predominance of the Arts course in the curriculum of the student training for medicine was thus explained by its origins. The original purpose of all education was merely to train clerks for service in the Church, and the chief Faculty was naturally that of Theology. Only later, as more secular control of university education became general, did the Faculties of Law and Medicine increase in importance as alternatives. The basis in all three remained, however, the original liberal arts, which had to be studied before the student could be licensed to the degree of Master of Arts. After this he was then free to enter the Faculty of Medicine where a similar period of study would result in the degree of M.D. At the beginning of the Tudor period each student was expected to enrol himself with an M.A. who would act as his tutor. As the collegiate system developed official tutors were appointed, and the more elementary aspects of such instruction were gradually delegated to the new grammar schools and excluded from the university curriculum (1549) in similar fashion to what has happened with the pre-medical subjects in our own time.

In certain circumstances a dispensation might be granted by the Congregation of Regents to reduce this preliminary period of seven years on the production of evidence of sufficiently meritorious study previous to joining the university. That this procedure must have been sometimes abused, however, is shown by the celebrated case of the Franciscan monk, Simon Ludford, who although subsequently proved illiterate was granted an Oxford B.M., an event which provoked a violent protest from the College of Physicians of London.

Oxford and Cambridge at this time provided very little systematic and no practical medical teaching; consequently comparatively few troubled to seek their qualifications: it would seem that the examiners at Cambridge only required candidates to read and expound certain of the works of Hippocrates, Galen and the Arabist Aretæus. They considered only the basic intellectual needs of the physician, and were actively hostile to any form of practical teaching, which had to be sought elsewhere. It is interesting to note, however, that the first

scholarship ever endowed in England, by Archbishop Parker, was to be tenable by a student of medicine at Caius College, Cambridge; whilst in 1581, under the Statutes for the Lumleian lectureship of the College of Physicians, a two years' travelling Fellowship abroad was envisaged. It was more usual, after spending the requisite seven years obtaining the M.A., for the student to proceed to one of the continental universities, where the teaching was renowned, and after obtaining his M.D. to return and "incorporate" this in his Alma Mater. The course of study and the required textbooks were similar all over Europe, where the formal lectures were still a strange mixture of alchemy, medicine, magic and astrology based on complete confidence in the teaching of Galen, and later Hippocrates. As a contemporary said "Physic without astrology is like a lamp without oil".

Travel did not present much difficulty to scholars in the early Tudor period, particularly if they were in priestly orders and therefore polylingual. With the great growth of commerce during the reign of Henry VIII mail and carrier services with the Continent were efficiently organized, and only rarely were complaints heard until the next reign, when more troublous times and wars with France returned. From Calais there were direct and frequent services both overland and by sea to Antwerp, Bordeaux, Spain and Venice. Sea passages were the most expensive and had to be paid in advance, whilst, as is often still the case, the merchandise was considered to take precedence of the passengers. It was not until these routes were closed as the result of Henry's wars and the additional disruption of trade which followed devaluation of the coinage in 1551, that our own universities really began to recognize their teaching responsibilities. Nevertheless, the tradition that "A Physician must be a traveller" continued to survive throughout the Elizabethan era. As Thomas Coggan (1545-1607) says "If one will know many diseases he must wander far . . . not merely to describe countries as to how they wear their breeches, but courageously to attack the problem as to what kinds of diseases they do possess".

English teaching.—In England it was Dr. Caius who was chiefly responsible for the growing contemporary realization that it was the new anatomy of Vesalius that could provide the chief factual basic science for medicine. He started his systematic lecture-demonstrations on the subject at the Barber-Surgeons' Hall in 1546, and in Cambridge in 1557. It was not until eight years later that the College of Physicians also gained the privilege of collecting annually

the bodies of up to four criminals, after which each Fellow under penalty of a fine had to give a public demonstration and lectures.

Beside medical teaching had long been introduced by Montanus in the hospital of St. Francis of Padua, and pupils from all countries flocked there to attend. It seems strange that Caius, who was of their number, made no attempt to transplant this, and in consequence the system did not reach England until the next century. There were, however, no hospitals of consequence in England at that time, with the exception of St. Thomas's and St. Bartholomew's in London, and these were still largely only shelters for the poor. For many years therefore the practice of medicine had to be learnt by apprenticeship, either before or after qualification. In England it was in fact still not generally considered necessary for the physician to see his patient for the purpose of diagnosis or treatment, although under the influence of Linacre the College of Physicians in London was beginning to give teaching on more enlightened lines and decrying the ancillary diagnostic aids of astrology and urinoscopy.

Since medicine and magic were still inextricably intertwined, however, anatomy and astrology still continued for many years to be regarded as two equally important facets of the same science. The medical student, when taught the therapeutic virtues of herbs, was also taught to pluck them under the right aspects; whilst he was of course well aware of the influences the planets and stars were supposed to wield upon the bodies and affairs of men.

The rebirth of interest in medical education in Oxford and Cambridge did not develop fully during the Tudor period. It was somewhat stimulated by Linacre's endowment in 1524 for six solemn lectures to be given every year at Merton and St. John's Colleges; and also by the establishment at both universities of Regius Chairs by King Henry VIII, himself no mean amateur in physic. Until quite late in the Reformation, however, both Oxford and Cambridge remained under predominantly clerical influence, and the medical education such as it was continued to consist only of reading and exposition of the classical theoretical works. As Michael Foster said "The Church still held the gates of learning, and they who entered were bidden to tread her path, and hers alone . . . it narrowed itself to asking what the old teacher had taught"—the doctrine of "Magister Dixit". To remedy this state of affairs Edward VI sent a Royal Commission which proposed (1549) that one of the Colleges of Cambridge should be taken over by the Faculty of Medicine and used entirely as the "King's Medical College". This

was not done, but nine years later Dr. Caius endeavoured to fill the deficiency by refounding Gonville Hall, under Royal Charter, and making special provision for the study of medicine. This included two medical Fellowships and later (1564) a formal grant from Queen Elizabeth of two bodies annually for dissection by the students without fee. It would seem that unfortunately very inadequate use was made of these advanced facilities until the seventeenth century.

European teaching.—Montpellier, at the opening of the Tudor period, was still the leading medical centre of the civilized world, and many English students resorted there, as in all other European universities their M.D. degree would have involved them, if already holders of an Oxford or Cambridge M.A., for a period of five to six years' study. Only half of each year was actually occupied by the formal course of lectures and disputations, but they must during this period have joined in at least two of the latter in public. The other half of each year was to be spent in travel and practical treatment of the sick under the supervision of some "famous" doctor. Custom began the day much earlier then, the usual hour of the first lecture in most universities being 5.0 a.m., which lasted until 10.0 a.m.; then half an hour was allowed to correct notes, after which came the communal dinner; lectures recommenced at 1.0 p.m. to 5.0 p.m., supper was provided at 6.0 p.m., and the latest official hour for retiring to bed was 11.0 p.m. The university fees (bourse) were assessed according to the apparent resources of the student. These were payable weekly and included books and tuition, and in some cases also food and necessary clothing.

The books it was laid down that he must read, and later be examined on, were a large proportion of the works of Galen and the Aphorisms of Hippocrates, Dioscorides on simples, and certain of the works of the eleventh century Spanish Jew Isaac (particularly his work on Fevers and the "De Dictis Universalibus"); also either the Canon of Avicenna or Rhazes, since Montpellier retained a veneration for the Arabists long after the rest of Christian Europe was in revolt against them.

In the "lay" universities of Bologna, Padua, Pisa and Pavia, where Chairs of Anatomy subsidiary to that of Medicine had been installed, human dissections had been carried out in spite of the active opposition of the Church, on the bodies of executed criminals since the middle of the thirteenth century. Thence the practice spread through the rest of Europe, being legalized in Montpellier in 1377, where the Faculty of Medicine initiated five to six dissections annually.

These were public, but the students of medicine were admitted for a much lower fee. In Paris, which remained under ecclesiastical domination, human anatomies were not permitted until 1551, as it was considered that no such disrespect must be paid to the temple of the soul which is the body.

Surgery.—Oxford and Cambridge made little or no provision for the teaching of surgery, which having formulated no general principles was regarded all over Europe as a craft somewhat beneath the notice of a university graduate. Montpellier was exceptional in its outlook, however, and at times supported a subsidiary Chair of Surgery in the Faculty of Medicine. Its famous Dean, Joubert, produced a translation in French of Guy de Chauliac's classical Arabist textbook "for un-Latined surgeons and apprentices" and deplored "the debasement of this most excellent and ancient part of medicine—the most excellent of all in respect of the results it has to show". Fernel in the preface to his "Pathologica" (1554), which had great influence throughout Europe, said also "Surgery is one with medicine, it rests on the same principles and follows the same essential ideas", but he thereby incurred the official censure of the Paris Faculty for what was termed gross disloyalty to his cloth.

Academic standards for the surgeon did not exist in England until the union of the Fellowship of Surgeons with the Barbers' Company as the United Company of Barber-Surgeons in 1540, although the former did examine applicants for their Guild as early as the mid-fifteenth century. Formal oral examinations, however, now were instituted for the Licence, which they were authorized under their Charter to award. The set books for this were the Anatomy of Realdus Columbus (1530), together with certain parts of Galen's works, "De Methodo" and the "Therapeuticon", which had been newly translated for this purpose by their Reader Dr. Caius; the English translation of Guido's "Questions" (1544), Tagaultius' and John of Vigo's Surgery (1514); and later the writings of their Masters, Thomas Gale, Thomas Vicary, William Clowes and others. The works of Paré were known and appreciated, but were not translated into English until 1634. Practical anatomy was also taught by means of dissections of the cadaver under the direction of the Reader. This was done by systems and not by regions, as is still the practice in veterinary anatomy, as bodies were fairly plentiful and no preservatives were known. The most perishable parts, the viscera, were the subject of the first day's lecture; the second day was spent on the muscles and arteries, whilst on the third and last day the discourse was of the bones, ligaments and joints. This practical

course was held at least annually and sometimes more often, so that the student apprentices had the opportunity of attaining quite a good knowledge of anatomy during their seven years' period of servitude.

Medical textbooks.—Throughout Europe medical knowledge was originally derived from the writings of the great Greek philosophers Aristotle and Hippocrates and their Græco-Roman successors Galen, Dioscorides, Paulus Ægineta and Celsus. These men and their disciples were considered to be infallible monopolists of all true scientific knowledge for over a thousand years.

After the fall of the Roman Empire learning went out of Europe, but the new Arab Empire inherited and preserved in translation much of this learning. The Greek gold they transmuted to baser metal, but their great physicians Avicenna and Rhazes made some further contributions to clinical knowledge. When in the twelfth century they captured Southern Europe, and so created the Western Caliphate, all these works were reintroduced but mostly in debased Latin translations which from then constituted the corpus of mediæval medical learning, and were the standard textbooks in all the universities. An indigenous school of independent medical thought, however, developed in Spain and produced several outstanding figures of whom the best remembered to-day are Averroes (1126–1198) and Isaac the Jew (Isaac Judæus, 845–940), whose collected works remained "required" reading until the eighteenth century.

The works of Galen covered every field of the practice of medicine and surgery, and became the ultimate authority throughout the Middle Ages and Renaissance, and were taught as a rigid system from which it was heresy to depart. Although he was a man of overwhelming vanity, his mind was critical and this cult would in all probability have been distasteful to him. The pure texts of his works were introduced into England through the translations of Linacre and Caius. His contemporary Dioscorides was a Greek doctor who served in the Roman Army during the reign of the Emperor Nero. His great "Materia Medica" remained authoritative until the seventeenth century and is one of the textbooks mentioned by Chaucer's Doctor of Physicke. Another physician of the later Greek period whose works were "required" reading for the students at Oxford and Cambridge and elsewhere was Aretæus, the Cappadocian (first century), who gave quite good accounts of pneumonia, empyema, diabetes, tetanus and insanity, and pointed out that in hemiplegia

paralysis occurs on the side opposite to the brain lesion. Pharmacology was covered by the "Antidarium" of Nicholas of Salerno in all universities.

Celsus, who was referred to as "the Latin Hippocrates" by Dr. Caius, was a nobleman who lived on his estates near Rome and set himself the task of epitomizing all contemporary science, chief amongst which—unlike his contemporaries—he rated medicine, both human and veterinary. In his fourth book he enumerated the four classical signs of inflammation—*rubor*, *dolor*, *calor* et *tumor*. Paulus Ægineta who wrote also on surgery, was a Byzantine physician of the seventh century, the sixth book of whose eight works constituted almost the complete opus of surgical lore in Europe until late in the Renaissance when the extensive use of gunpowder outdated the sections on military and traumatic surgery. He gives what appear to be original descriptions of lithotomy, paracentesis, tonsillectomy, amputation of the breast and eye surgery.

The Arabian physician Avicenna who was born in 980 is described as an arrogant, youthful prodigy who at 18 pompously claimed to be the repository of all knowledge. His "Canon Medicinæ", which Osler called the most famous textbook ever written, exerted an influence second only to that of Galen himself throughout the thousand years of darkness. His contemporary, Rhazes, also published a great encyclopædia of medicine, the Latin translation of which weighed over 22 lb. The Caliph with whom he had quarrelled ordered him to be beaten on the head with this, which may have caused his early blindness. Smallpox and measles are for the first time clearly differentiated in this.

The Arabian school of medicine, of which these two men were the chief ornaments, alone tended the lamp of intellect in Europe during the Middle Ages, although with the coming of the Renaissance their light was extinguished by the recovery of the original Greek manuscripts upon which their works had been based. These were reintroduced by fugitive scholars after the fall of Constantinople, and made available to the learned in England through the translations of the scholar-physicians whose leader was Linacre.

Printing.—Until the invention of printing the diffusion of knowledge was by means of manuscript copies of the works of the old Masters, and by attendance at the lectures and discourses of the teachers in the various universities of Europe. The Church, which had control of most of these seats of learning, had an organized system for the production and exchange of manuscripts amongst scholars, and at first opposed printing as it interfered with this profitable trade.

Amongst students throughout the first few years of the sixteenth century, printed books tended to be expensive and scarce, and manuscripts to become steadily less available in England. Whole classes would subscribe for the purchase of a chosen textbook which would be read aloud by the teacher so that they could memorize it by repetition. To facilitate this these were often written in rough verse. One of the first and most popular of such books was the "Regimen Sanitatis", which was the traditional textbook of the first medical school to be established in Europe in the Italian town of Salerno. The best Elizabethan translation was made by Queen Elizabeth's erratic but gifted godson Sir John Harrington, who also invented the water closet.

The multiplication of printing presses soon made textbooks more available for the individual student, and in most Faculties they also became gradually less unwieldy and expensive as, other things being equal, a smaller size implied a smaller price. It was the celebrated printer Aldus (1450–1515) who first produced books of size for the pocket and made a fortune. The exception was legal textbooks which remained huge and stuck to Gothic type, so that when produced in Court they might impress the unlettered laity with the learning of their owners!

The growing impatience of the early Tudor intellectuals with the obscure and sterile scholastic subtleties of their European and Arabic predecessors led the new commercial printers to subsidize an orgy of simplifying, epitomizing and classifying of available knowledge for the benefit of a wider class of student. They soon began to pour out a spate of what would now be called "Aids to Medicine"; second-hand compilations based upon incorrect versions of the classical authors, which tended to spread a little learning over a larger section of the population. Unfortunately the basic works which were most readily available for this treatment were the popular but obsolete mediæval textbooks such as "Rosa Anglica", which Andrew Boorde designated as "a verie stynkyng Rose"—no doubt fair comment on one best-seller by the writer of others, and "Lilium Medicinæ"; and so it tended to be the old learning which was in fact perpetuated in this new and receptive field for almost another century. A further factor which worked to the detriment of the new learning was the high cost of printing; even such a monumental work as Fernel's "Universa Medicinæ", which had been used in manuscript as a textbook in all universities of Europe for over half a century, was only printed posthumously in 1567. The fact that this was still worth while, however, shows that the science and ideas of the earlier period had not changed basically.

Amongst the mediæval textbooks which enjoyed this St. Luke's summer of popularity in England were the works of the learned Oxford Prebendary and doctor, John of Gaddesden, the first Englishman to be employed as Court physician. In his "*Rosa Anglica*", mentioned above, he systematically but unscientifically lists all diseases "*a capite ad pedis*", and it is typical of the period that both rational treatment and cabalistic charms receive equal recommendation. Another reason for its popularity may have been the "list of diseases which will bring to the doctor the most monie". William Gilbert (Gilbertus Anglicus), who was probably a medical officer to the third Crusade, wrote "*Compendium Medicinæ*" which, in addition to the practical summary of contemporary medical knowledge which it contained, was consulted by the laity on account of the hygienic and other directions for travellers abroad with which it concludes.

The works of the two great fourteenth century surgeons, Guy de Chauliac's "*Chirurgica Magna*" which was first printed in 1478, and John of Arderne's "*De Chirurgia*", also continued to be basic reading until the end of the Tudor period. The latter is the first English surgeon of whom we have record. He was educated at Montpellier, was present at the battle of Crécy, after which he was given an estate by the Black Prince whose piles ("*fistula*") he had cured, and later practised general surgery and proctology with great success. Unlike his successors he strongly advocated clean hands and well-trimmed finger nails for a surgeon.

The earliest popular pharmacopœia to be printed was the "*Antidotarium*" of Nicholas of Salerno (1471) followed by the "*Nuovo Receptario*" at Florence in 1498.

The dawn of the Renaissance in Northern Europe coincided with the opening years of the Tudor period in England, where a new type of author arose, of whom Sir Thomas Elyot and Dr. Andrew Boorde are the best known. These men, although never doubting the bases of Galenical theory, tempered their writings with the first records of personal experience and sceptical good sense, and wrote not in Latin but in their native tongue. They also laid the foundations of hygiene and Public Health. Boorde's "*Dyetary of Health*" and "*Breviary of Health*" (1542) are the first medical works to be written by an English physician in the vernacular, and they continued to be best-sellers for long after his death.

In spite of the eclipse of the Arabists the learned Tudor physician would still be conversant with the works mentioned by Chaucer in his "*Doctor of Physicke*", as the sources of his hero's knowledge. This list includes six Arabians and

four Arabists. The academic reaction in favour of neo-platonism with its more enlightened methods of thought was for several decades confined to the medical humanists whose interest in the new Greek manuscripts was largely directed to their literary aspects. Thus the old works continued to be printed and circulated for many years.

The most important of the medical fruits of the Renaissance were contained in such works as Vesalius' great "*Fabrica*" (1543) in which was epitomized the new science of anatomy with the wonderful illustrations by Titian's pupil Calcar. This was so expensive, however, that he shortly afterwards published the "*Epitome*", but even this was not translated into English until 1553.

The greatest physician in Europe at this time was Jean Fernel (1497-1558), who alone of the academics of this period realized that the chief need of medicine was not, as most of his contemporaries thought, to recover the purest Greek original texts, but to sift facts from the many uncertainties and legends with which the subject was literally bedevilled. Medicine had but few solidly demonstrated truths, and the literary physicians of the Renaissance troubled very little regarding this as they mostly found themselves able to accept large portions of the occult mixed up with the "laws of Nature" as they interpreted them. Fernel in his great work "*Universa Medicina*" (1554), omitted almost all mention of astrology and alchemy to the great surprise of the Faculty in Paris who thought it reactionary, and indeed presumptuous, to eschew help from the stars which had been arranged for that purpose by a beneficent deity. He was a skilled anatomist who influenced Vesalius, and he was the first to formulate the science of physiology as a necessary introduction to medicine and to call it by that name ("*physiologica*"). His book remained the chief textbook of the Medical Faculties of Europe until the end of the seventeenth century. Unlike most writers of that time—who scorned to pay much attention to the local sites of disease, since for them every disorder from boils to disappointed love stemmed from an imbalance of the humours—he considered the body organ by organ. In the absence of the experimental method he was unable to re-found medicine upon any sounder basis than the humoral system; none the less, by his rational approach he cleared the ground for Harvey, and Sherrington has referred to him as "the John the Baptist of Physiology and Medicine".

Towards the end of the century the works of Paracelsus (1493-1541) began to appear in translation in England. These produced a tremendous impact. Paracelsus, who had had a

great contemporary reputation as a clinician, was original and rich in ideas; Thorndike considered him to be half genius, half charlatan. Sudhoff refers to him as "the eccentric father of chemistry and the reformer of *Materia Medica*", which epitomizes his achievement in introducing mineral substances such as mercury, arsenic and iron as well as laudanum and tinctures into medical treatment, and stirring up "divine discontent" with the prevailing humoral system.

Subsequent to John of Arderne, whose mediaeval works have already been referred to, the English surgeons did not begin to write books until the Tudor period was well advanced and the Company of Surgeons had been incorporated. This event led to a need for native primers which were, however, mostly the mediaeval favourites "modernized" in new guise and under new names. It was not until 1563 that Thomas Gale, Master of the Company, published his textbook in three parts. The first was the "Institution of a Surgeon" which took the novel form of question and answer between three friends: the second "The Enchiridion, or Manual of Surgery"; and the third "An Excellent Treatise on Gunshot Wounds, and the Office of a Surgeon", which had been published separately in 1536 and so constituted the first surgical textbook in English. Other works were Thomas Vicary's elementary treatises written for his apprentices "A Profitable Treatise of the Anatomie of man's body", and "The Englishman's Treasure" (1548) which was the first native anatomical textbook. These were all written in English: as Gale says in his preface "Foreasmuch as there be many younge men desirous of knowledge in this arte, and fewe of them learned in the Latine or Greeke tongue, Therefore I with the helpe of my friends, have set forthe these bookes in Englishe". In 1575 William Clowes translated the seventh book of Fernel's "Pathologica" which dealt with surgical procedures; and three years later appeared John Banister's "Historie of Man", which remained the best textbook of surgical anatomy until the modern period.

In Scotland Peter Lowe broke new ground by publishing "A Discourse on the whole arte of Chirurgie" in 1596; this was the first textbook on surgery to be written specifically for the use of students who were going to be examined in the subject. He also translated certain of the works of Hippocrates into English for the first time (1597).

Qualification.—Academic medicine remained a purely scholastic exercise throughout Christian Europe until the introduction of bedside teaching in Italy during the sixteenth century, on the pattern which had long been familiar in the

Moslem Empire. This did not reach England until the seventeenth century, however.

Although the Faculties of Medicine at Oxford and Cambridge were as old as those of Divinity and Law, lectureships in medicine had always been considered as sinecures, and medical teaching in England had therefore sunk to a very low level by the reign of Henry VIII. Very few degrees were given, although foreign degrees were frequently "incorporated" "*ad eundem gradum*" for the appropriate fee, by men who had previously taken their Mastership in Arts in Oxford or Cambridge and had obtained their M.D. abroad. This plan was possible owing to the fact that all European universities were, at any rate theoretically, under the same religious authority, and so the permission to teach, which a doctorate implied, was equally valid in all, wherever the degree was actually conferred: "*jus ubique docendi*". The doctors of the superior Faculties of the universities therefore constituted the aristocracy of the intellectual hierarchy of Europe. Until 1511 the medical degree of a university provided the only legal qualification to practise in England; in that year the Bishop's licences in medicine and surgery were introduced, whilst the College of Physicians, after its formation in 1518, was also empowered to confer licences to practise within the City of London and within a radius of seven miles, and the Act of 1522 extended this power to the whole country.

Examinations.—The aspirant to the M.D. in Oxford and Cambridge, as in most universities of Europe, was examined for his M.A. after seven years of study in grammar, rhetoric, logic and philosophy, as well as theology. Philosophy would include a knowledge of all natural phenomena and particularly of the stars. In Oxford and Cambridge under the Statutes of Edward VI a student who had then proceeded to the Faculty of Medicine and had witnessed two anatomies could, after four years of further study, face a Board composed of four Regents who would decide whether he was by then a fit and proper person to "determine". This was a process which lasted several days during which the candidate had to defend a thesis against all comers. If successful he could claim to receive the degree of Bachelor of Medicine from the Chancellor of the university, and permission to practise within the municipality was granted. He was now regarded as a pupil-teacher, and was expected to give certain "cursory" lectures to junior students, whilst continuing his own studies for a further four years. At the end of this period he would need to produce evidence that he had performed two anatomies himself

and had effected three cures (Ed. VI Statutes 1549). He could then undergo the final act of inception, disputing with other candidates before a Regent in Medicine, who would if he approved him, lead him before the Chancellor and give a personal account of his character and attainments. After this he must take the customary oaths and be approved by the other nine Regents *nem. con.* His final admission into the ranks of the Doctors would take place in the university Church, and after this, accompanied by the university Bedel he was expected to pay a round of visits to all the Regents, inviting them to his banquet. For the next two years he would normally serve as a Regent himself, giving weekly lectures to students.

It was possible in some continental universities after graduating as M.A. to achieve the licence to practise in a shorter period. In such cases the student would settle in the city where he could attend the lectures and discourses of the most celebrated physicians, and after two or three years would enter for the four tests of knowledge known as "per intentionem". Four different professors would interrogate him each on a different malady, verbally—for written examinations were only introduced by the Jesuits a hundred years later—and eight days later he presented himself before the Chancellor to "prick" his great volume of the Aphorisms of Hippocrates in order to decide by chance the fifth disease on which he would be examined in public on the next day. Previously, however, he would have delivered a thesis or dissertation before the Dean of the Faculty on some subject "on which he had pondered for not less than two days". In Montpellier all this used to take place within the Church of Notre Dame-des-Tables between the hours of midday and 4.0 p.m., the examination being always conducted in the form of a dispute between the candidate and the Professors of the Faculty. The former was expected to parry the questions and avoid the verbal traps with which the latter would beset him, since learning at this time was accounted largely a matter of memory for the appropriate citation, combined with a nimble wit. A week later, if he proved successful and could produce evidence of experience as an apprentice to some "famous doctor", he would receive from the Bishop himself "in aula episcopali" his licence to practise, which was designated "Ad practiciandum in Medicina [or Chirurgica] per Universam Anglicum", and was of a lower standard than the full university degree.

It was possible to proceed further to the M.D. after surviving a whole new series of public examinations of a very high order which lasted three days and nights, on the final day of which

the candidate had to sit in the Church and answer publicly all questions appertaining to some "chosen" subject. Next day musicians would call at the lodgings of the successful candidate and precede him, wearing his new robes and accompanied by all the members of the Faculty, to the Church of St. Firmin where the square cap of the Doctorate and a ring and a girdle of gold were placed upon him by the Chancellor, who also presented him with a bound volume of the works of Hippocrates.

For the *English licences*, under the somewhat anachronistic Act of 1511 (3 Hen. VIII), the Bishop of London or the Dean of St. Paul's was authorized, with the assistance of four physicians or surgeons of good repute chosen by himself, to approve candidates who were not university graduates, to practise without prejudice to the ancient rights of Oxford and Cambridge. Outside London the diocesan bishop or his Chancellor had the same power, but as they often found it difficult to assemble an expert panel of this sort in the country they were entitled to request the President of the College of Physicians and his three "Elects" to act in their personal capacity for them. The usual standard required of candidates for these licences to practise "in nomine Domini" appears to have been low, and they were widely distrusted. The connexion between physical and spiritual sickness which was implied in this practice was generally recognized, and the still powerful Church felt that it was fitting that such practitioners should be admitted under their control. Thus it is easy to see why Henry VIII in his enlightened desire to institute a National Health Service which should extend over the country, should choose as his medium at this time the efficient organization of the Church which reached everywhere. Moreover the bishops were the State officials most likely to detect and be able to punish the more flagrant quacks.

With the establishment of the College of Physicians in 1518 these licences were to some extent superseded in and around London by those which the College was now authorized to grant, although the Act was only actually repealed in 1948! For candidates proposing to reside in the City the standard required was quite high, but it was considerably less rigorous for those in the country. The licentiates who obtained in addition the requisite "letters of testimonial" were entitled "Candidates of the College". This was roughly equivalent to the modern M.R.C.P.; and after a probationary period they could be advanced to the Fellowship. The required reading was all contained in the works of Galen, with the exception of the "Aphorisms" and "Prognostics" of Hippocrates—these works had

recently been made available by the fine translations of the President of the College, Dr. Linacre. There were four examinations, held in public by the President and Fellows over three days, and for the first time in England candidates were also now examined in the practice of medicine. They would be asked questions as to when, to whom, and in what cases should purgatives be given, or blood letting practised; what care was to be taken in the administration of soporifics and narcotics, and the nature, measurement and use of clysters. The Statutes stated, however, that "we wish that Fellows shall not show themselves pedantic or difficult" in their questioning. The claims of the Church to dominate medicine as expressed in the earlier Act were not accepted by the College, in which an anti-clerical bias developed in consequence.

In 1534, at the Reformation, the Crown granted to the Archbishop of Canterbury the right to confer degrees in certain subjects, including medicine, subject to the monarch's approval, although it did not automatically include the right to practise. This was a remnant of the Papal authority and was transferred merely for prestige reasons to the Church of England, when Henry assumed the title of "Supreme Head of the Church and Clergy as far as the Law of Christ will allow". These so-called Lambeth degrees can still be awarded in certain circumstances.

Although the Barbers' Company instituted an oral examination in 1493, it was not until after the official union of the Fellowship of Surgeons and the Barbers' Company in 1540 that a systematic if rudimentary examination of their apprentices was instituted at the end of their period of servitude, before they could receive their freedom and their licence to practise. After the apprentice had presented a recommendation from his Master, he was presented to the Master of the Company and examined orally in the presence of the full Court by four selected surgical members of the Company. If his replies were considered satisfactory he would be given leave to "hang out his pole", after paying a fee of viii d. to the Company, a donation to the poor-box, and the Clerk, and a tip to the Bedel. The Company also instituted "The Great Diploma", a higher degree which entitled the recipient to the prefix of "Master" in surgery and

anatomy. The fee for this was seven guineas in cash, a silver spoon weighing not less than an ounce, and viii d. to the Clerk for enrolling him. This officially ended the confusion as to who outside the ranks of the College of Physicians might legally practise the art and craft of surgery.

It is interesting to note that some postgraduate education was also enforced by the regulation whereby all licensed members of the Company, including the Master and Wardens, had to attend the lectures on surgery and the anatomy demonstrations. Exemptions from this were rarely granted and then only upon the payment of a fine of twenty shillings.

To summarize, the only legal basis for practice at the outset of the Tudor period was the possession of an M.D. which took fourteen years at either Oxford or Cambridge. These universities were extremely somnolent and being still under close ecclesiastical domination remained largely immune from the influences of the Renaissance. Since, however, at that time the educational system was universal, the brighter medical students, after taking their M.A., would travel to one of the "free" universities of Europe to take their M.D. and return home to "incorporate" it. In view of the small number of these medical graduates an Act of Parliament was passed in 1511 whereby licences to practise medicine or surgery could be issued by bishops, and again seven years later the College of Physicians was authorized by its Charter to do the same. All medical education at this time, however, was entirely theoretical and practical experience had to be gained by apprenticeship either before or after qualification.

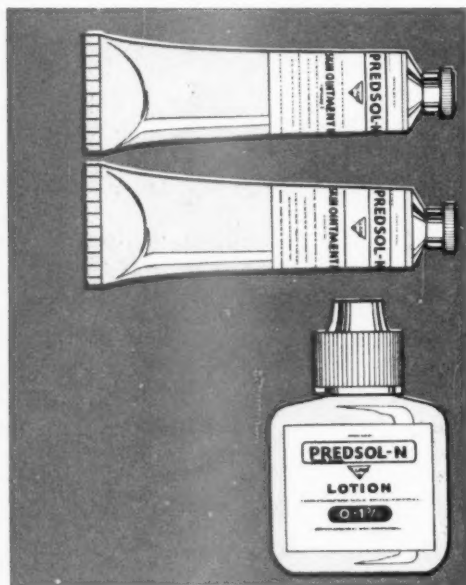
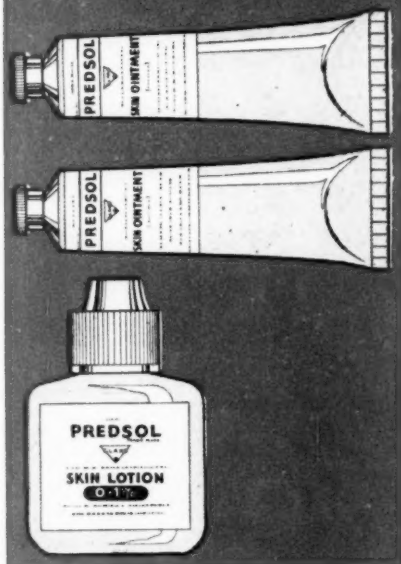
No provision was made for surgical education until 1540, as this was rated as a mere craft unworthy of the consideration of medical graduates. In this year, however, the Company of Barber-Surgeons was chartered and a system of professional education was evolved for its apprentices before they could be licensed to practise.

In view of the intellectual stagnation of the university Medical Faculties, the College of Physicians, under the stimulus of Linacre and later Caius, introduced the new learning of the Renaissance and successfully took the lead in the development of medical education in Tudor England.

Meeting
May 6, 1959

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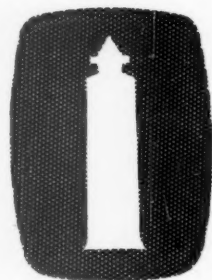
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Meeting
February 6, 1959

Intermittent Positive Pressure Respiration. Some Physiological Observations.

By A. CRAMPTON SMITH, M.B., F.F.A. R.C.S., and J. M. K. SPALDING, D.M., M.R.C.P.
Oxford

Dr. A. Crampton Smith:

The control of the ventilation of paralysed patients receiving intermittent positive pressure respiration is in the hands of the doctor in charge of the patient, and it is no less difficult than it is important to maintain ventilation at suitable levels.

An accurate, easy, and rapid means of assessing the effect of the chosen ventilation would be of great value to the clinician, and I should like to describe what we have done in this direction and to show some interesting by-products of our studies.

It gives me pleasure to acknowledge the assistance we have received from Drs. D. J. C. Cunningham and B. B. Lloyd of the Department of Physiology of the University of Oxford and I should like to thank Professor Sir Robert Macintosh for help received from the Nuffield Department of Anaesthetics.

Apart from the measurement of the volume of expired air, the two most commonly used methods of assessing the adequacy of ventilation are, first, the measurement of the $p\text{CO}_2$ of blood and, second, the measurement of the $p\text{CO}_2$ of end-tidal air. Both methods have advantages and disadvantages. Blood gas analysis is discontinuous, and can only reflect the situation existing when an arterial sample is taken. The actual estimation in blood is delicate, especially in respect of the measurement of pH, where a small error is magnified in the method of calculating $p\text{CO}_2$. End-tidal air samples are easily, and can be continuously, obtained, and may be analysed in various ways, some of which are quite simple.

It has been shown by Suskind and others (Suskind *et al.*, 1950; Galdston *et al.*, 1951; Saxton, 1953) that in the normal subject, that is the subject who is not paralysed, has normal lungs, and who breathes spontaneously, the $p\text{CO}_2$ of end-tidal air bears a close relationship to that of arterial blood. Walley (1957), however, has shown that in patients who have radio-

logically recognizable changes in their lungs, and who are receiving artificial ventilation—in whom it is particularly important to be able to assess the adequacy of ventilation—there may be a considerable difference between end-tidal and arterial $p\text{CO}_2$. It has also been shown (Campbell *et al.*, 1958) that in patients who are anaesthetized, and in those receiving artificial ventilation, there is a smaller and more constant discrepancy which is ascribed to maldistribution of the ventilating gases in the lungs.

So one apparently has to choose between the error of blood gas analysis, which we believe to exist except in the hands of the practised expert, and the error in end-tidal analysis induced by pathological states which lead to uneven ventilation and to an arterio-end-tidal gradient.

Hackney *et al.* (1958), describe a technique involving only gas analysis, which gives an indirect estimate of the arterial $p\text{CO}_2$ with a standard deviation of ± 2.9 mm.Hg from that estimated directly from arterial blood; and this in patients with heart and lung disease.

The technique is directed to the equilibration of the $p\text{CO}_2$ of a gas mixture in a rebreathing bag with that of mixed venous blood. A fixed arteriovenous $p\text{CO}_2$ difference is subtracted to give the $p\text{CO}_2$ of arterial blood. It has been found that this factor is constant for wide differences of cardiac output. Campbell (1959) has, even more recently, described a modification of the original method which is much simpler. If the promise of this work is borne out, it would seem to be possible to use end-tidal sampling as an indication of change in our patient, while using a rebreathing technique to obtain more absolute values for arterial $p\text{CO}_2$. This would obtain even in the patients whom Walley describes, with lung complications and uneven ventilation.

We have used apparatus for end-tidal sampling and analysis in Oxford since 1954, as an aid to the assessment of ventilation, with due regard to its limitations in patients with abnormal lungs, and have found it useful. I feel, however, that rebreathing techniques may remove the reservations

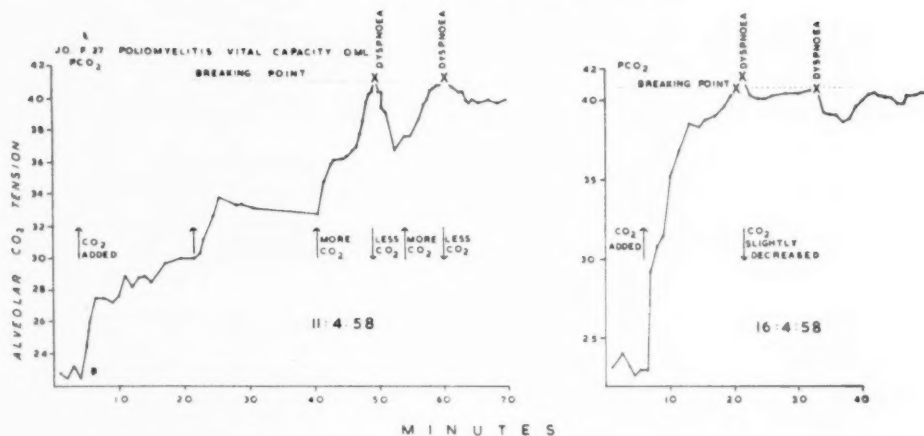


FIG. 1.—Effect of adding CO_2 to the inspired air of a paralysed patient on two occasions.

one has in respect of indirect methods, and we find this most encouraging.

We were fortunate in 1954 to find that the University Department of Physiology had already developed simple apparatus for the continuous analysis of CO_2 in air or oxygen. The analyser, originally described by Grove-White and Sander (1948) and modified by Cunningham *et al.* (1957), has a long response time, of about 60–90 seconds, but this has not proved disadvantageous when dealing, as we do, with fairly steady states. It has the advantages of being accurate, and almost free from drift. It requires only 60 ml./min. of gas and this in a minute volume of between six and ten litres does not materially influence ventilation.

Gases are supplied to the analyser by an end-tidal sampler. Where patients breathe spontaneously we use a Rahn-Otis sampler (Rahn and Otis, 1949) with a Cunningham-Lloyd (Cunningham *et al.*, 1956) valve. For artificially ventilated patients with a tracheotomy, we have designed a simple automatic "snatch" sampler which has been fully described elsewhere (Smith, Schuster and Spalding, 1959).

We have been interested, since we treated our first patient, in the fact that in our hands, and in those of others, patients on intermittent positive pressure respiration tend to be overventilated, judged both by measurement of the volume of expired air and by end-tidal pCO_2 . We are not by any means alone in observing that these patients often demand more and more air even when they are apparently more than adequately ventilated.

When parietic patients are removed from their

respirators and asked to breathe spontaneously, they may choose a lower or a higher pCO_2 on spontaneous respiration (Smith, Schuster and Spalding, 1959). According to Affeldt *et al.* (1955) the latter is the more usual.

In an attempt to find out a little more than this, we introduced CO_2 into the air drawn into the respiration pumps which were ventilating some of our patients. The end-tidal CO_2 was recorded.

A typical result is shown in Fig. 1. We were able to raise the CO_2 of end-tidal air from 23 mm.Hg to 40 mm.Hg without any complaint from the patient. At a pCO_2 of 41 mm.Hg she complained bitterly of acute shortness of breath from which she demanded immediate relief. This relief could be obtained by a reduction in end-tidal CO_2 of only 1 mm.Hg and was complete.

On another occasion, however, in the same patient (Fig. 2), the tidal volume was reduced, but not below the level at which it was expected to be adequate. Here, the patient felt shortness of breath at a much lower pCO_2 . This sensation was not so acute as that experienced in the previous experiment and could be tolerated for some minutes while 100% oxygen was substituted for air in the pump to exclude an anoxic drive. This made no difference to the sensation of shortness of breath.

Finally, on another occasion the same patient (Fig. 3) was given CO_2 until she complained of shortness of breath—her ventilation was then increased and this enabled her to tolerate a higher pCO_2 without discomfort. This work is reported in detail elsewhere (Smith, Opie and Spalding, 1959).

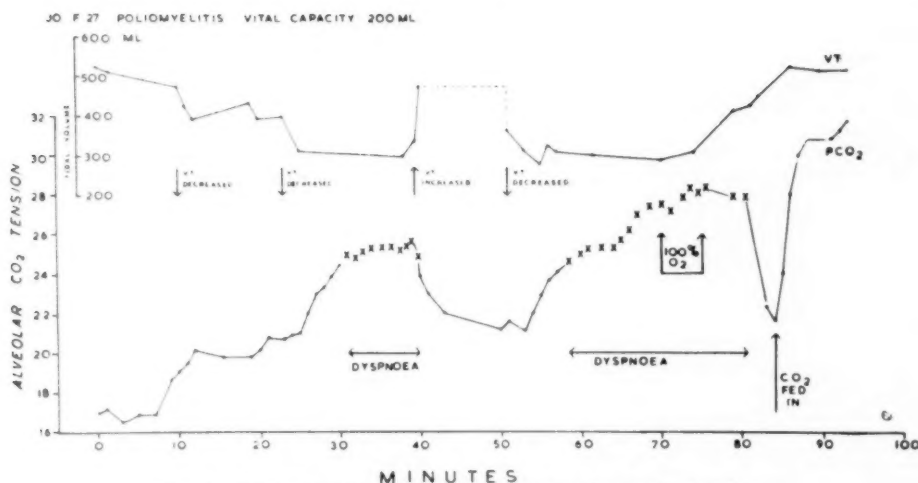


FIG. 2.—Effect of reducing the tidal volume (VT) of a paralysed patient.

The chemical control of ventilation is the subject of a vast literature. The possibility of other factors influencing ventilation has a smaller literature, but some of the experiments described are most ingenious. Affeldt *et al.* (1955) reduced the ventilation of parietic patients being ventilated in tank respirators until they complained of shortness of breath. They then opened the respirators and watched their subjects gain relief by spontaneous respiration in spite of a rising $p\text{CO}_2$.

Fowler (1954) made volunteers hold their breath to breaking point. They then respired from a bag containing a gas mixture with a $p\text{CO}_2$ roughly equal to their alveolar $p\text{CO}_2$ at the breaking point, and they thus obtained relief and could hold their breath again.

Mithoefer *et al.* (1953), in a particularly ingenious experiment, rebreathed from bags of varying sizes from 500 ml. to over 3,500 ml. in time to a metronome. These bags contained mixtures of CO_2 and oxygen. The breaking point in this experiment was taken as the point at which the subject could no longer hold his respiratory frequency to that of the metronome. Mithoefer was able to show that the breaking point depended not only on the $p\text{CO}_2$ and the $p\text{O}_2$ of the mixtures in the bags but also on the size of the bag or the tidal volume.

We have performed some simplified experiments along these lines which make rather more obvious the part of Mithoefer's work which we wish to emphasize. A subject respired 500 ml., 750 ml., 1,000 ml. and 2,000 ml. per breath of 100% oxygen at a frequency of 13/min., in time to a metronome. Increasing amounts of CO_2 were added to the inspired oxygen until the subject was forced by the sensation of shortness of breath to breathe more often or more deeply. This was regarded as a breaking point for each tidal volume, and the $p\text{CO}_2$ at the breaking point was recorded. 0.5 litres/breath 13 times/min. enabled the subject to tolerate a $p\text{CO}_2$ of 55 mm.Hg and 2 litres/breath 13 times/min. or a total ventilation of only 26 litres/min.

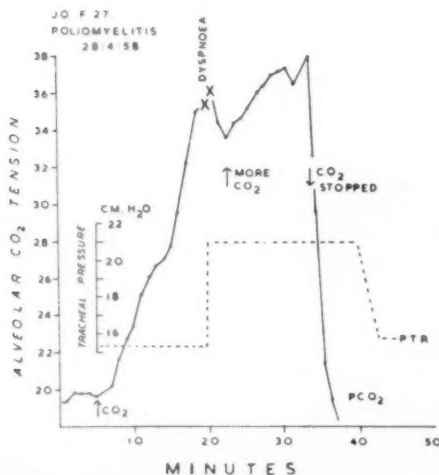


FIG. 3.—Effect of adding CO_2 and increasing the tidal volume in a paralysed patient.

enabled the subject to tolerate a $p\text{CO}_2$ of 77 mm.Hg.

From these investigations we have learned to appreciate the existence of an element of respiratory control which is interrelated with the effect of changes of $p\text{CO}_2$ and $p\text{O}_2$ and influenced by changes in ventilation—in our experiments achieved by alteration in tidal volume. Presumably these changes exert their effect through stretch receptors in the lungs or perhaps in the chest wall.

We have seen that our patients, when over-ventilated, are indifferent to an impressive rise in $p\text{CO}_2$ induced by CO_2 in inspired air. They do feel short of breath, however, with a comparatively small rise in $p\text{CO}_2$ —at very low levels of $p\text{CO}_2$ —if the tidal volume is reduced. From a practical point of view, it is clear that patients whose $p\text{CO}_2$ is lower than normal may nevertheless feel short of breath. We feel also, that the preparation of patients for weaning from a respirator must take into consideration not only the chemical control of ventilation, but also the influence of ventilation *per se*.

REFERENCES

- AFFELDT, J. E., COLLIER, C. R., CRAWIE, M. G., and FARR, E. F. (1955) *Curr. Res. Anes. Anal.*, **34**, 41.
- CAMPBELL, E. J. M. (1959) Personal communication.
- , NUNN, J., and PECKETT, B. W. (1958) *Brit. J. Anaes.*, **30**, 166.
- CUNNINGHAM, D. J. C., CORMACK, R. S., O'RIORDAN, J. L. H., JUKES, M. G. M., and LLOYD, B. B. (1957) *Quart. J. exp. Physiol.*, **42**, 294.
- , JOHNSON, W. G. H., and LLOYD, B. B. (1956) *J. Physiol.*, **133**, 32P.
- FOWLER, W. S. (1954) *J. appl. Physiol.*, **6**, 539.
- GALDSTON, M., BENJAMIN, B., and HURLWITZ, M. (1951) *Fed. Proc.*, **10**, 47.
- GROVE-WHITE, C. W., and SANDER, A. G. (1948) A Rapid, Sensitive, Continuous and Absolute Flow-bridge Gas Analyser. Report No. Chem. 422, R.A.E., Farnborough.
- HACKNEY, J. D., SEARS, H., and COLLIER, R. (1958) *J. appl. Physiol.*, **12**, 425.
- MITHOEFER, J. C., STEVENS, C. D., RYDER, H. W., and MCGUIRE, J. (1953) *J. appl. Physiol.*, **5**, 797.
- RAHN, H., and OTIS, A. B. (1949) *J. appl. Physiol.*, **1**, 717.
- SAXTON, G. A. (1953) *Fed. Proc.*, **12**, 125.
- SMITH, A. C., OPIE, L. J., and SPALDING, J. M. K. (1959) In press.
- , SCHUSTER, E., and SPALDING, J. M. K. (1959) *Lancet*, **i**, 277.
- SUSKIND, J., BRUCE, R. A. M., DOWELL, M. E., YU, P. N., and LOVEJOY, F. W., Jr. (1950) *J. appl. Physiol.*, **3**, 282.
- WALLEY, R. V. (1957) *Lancet*, **ii**, 1143.

Dr. J. M. K. Spalding:

When treating paralysed patients in the Respiration Unit at Oxford, Dr. Crampton Smith and I have often been appalled that we know so little either about the physiological changes caused by artificial respiration or about the factors that influence the patient's appreciation of its efficacy. In the last five years we have tried to make some measurements bearing on these matters, and we have found them helpful when considering clinical problems. Many people have helped us, and indeed we have helped each other, for anaesthetists and physicians—in this case neurologists—have worked very closely together and the benefits of this system have been obvious. I would like especially to thank Dr. W. Ritchie Russell for his encouragement, Dr. H. G. Epstein for technical advice and Dr. L. H. Opie for making many of the records.

My part is to summarize our recent findings in connexion with the *physical properties of the chest*, and first I must deal briefly with the measurements we make. Our records are made with a 4-channel capacitance manometer, and we record tidal volume, tracheal airflow, tracheal pressure and oesophageal pressure.

Our patients (Fig. 1) have a cuffed rubber tracheotomy tube (Spalding and Smith, 1956) with a grid-type flowmeter close to it in the tube leading to the respirator. Tidal volume is obtained by electrical integration of the airflow signal. The "tracheal" pressure is measured at the external end of the tracheotomy tube. The oesophageal pressure is measured through a polythene tube either with an air-filled system using a balloon 16 cm. long or with a water-filled system. The oesophageal pressure gives two types of information. In the first place it reflects the intrapleural pressure, so that we know from it the pressure applied to the lungs and to the chest wall respectively. The pressure exerted on the lungs is the difference between the intrapleural pressure and the tracheal pressure. Similarly the pressure exerted on the chest wall is the difference between the intrapleural pressure and the pressure applied to the surface of the body, normally atmospheric pressure. In the second place the oesophageal pressure is a measure of the mediastinal pressure and in particular of the pressure applied to the right atrium, so that the oesophageal pressure gives an index of obstruction to right heart filling during artificial respiration.

Results

The *elastic resistance* of the chest is the resistance that has to be overcome to keep the chest inflated to a given extent. It is measured when there is no air-flow in or out of the lungs.

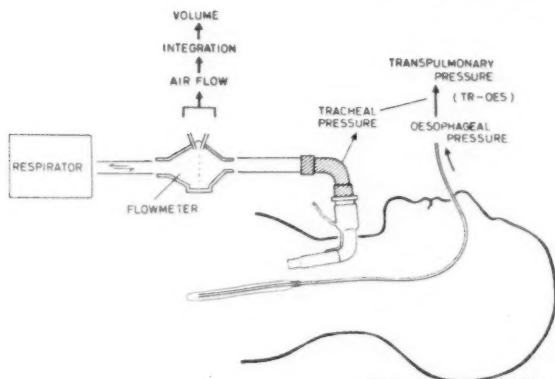


FIG. 1.—Patient receiving intermittent pressure respiration. Flowmeter, tracheotomy tube and oesophageal tube are shown.

It can be expressed either as the compliance, that is the volume that is held in the lungs by each cm. water pressure, or more directly as the pressure required to hold a given volume—conventionally 1 litre—in the lungs. The elastic resistance which we have found in normal, paretic and paralysed subjects is shown in Fig. 2. All subjects were supine, and the resistance in this position is somewhat greater than in the erect position. In the normal supine subject the elastic resistance of the lungs is about 7 cm. water per litre and our findings are in fair agreement with those of Attinger *et al.* (1956) and Howell and Peckett (1957) about this. The chest wall is moving actively so that it provides no resistance. In the paralysed patient receiving positive pressure respiration, however, the elastic resistance of the

lungs is much higher, about 19 cm. water per litre, and in addition the chest wall is paralysed and offers additional resistance of about 9 cm. water per litre. The marked difference in the elastic resistance of the lungs in paralysed and in normal subjects is of particular interest, and more information about it can be obtained by considering paretic subjects. In paretic subjects the elastic resistance is greater when the patient is receiving intermittent positive pressure respiration than when he is breathing spontaneously, both observations being made within a few minutes of one another. A similar phenomenon was found by Howell and Peckett (1957) who examined surgical patients and found the elastic resistance of the lungs greater when the patients were anaesthetized and paralysed than when they were breathing spontaneously. It is clear therefore that this difference is not due to a permanent anatomical change in the patient's lungs, and it is likely that it is due to an abnormal distribution of inflation of the lungs with artificial respiration. There is independent evidence of this in the existence of an abnormally high gradient of CO_2 pressure between the alveolar gas and the arterial blood in intermittent positive pressure respiration, but I am uncertain whether this abnormal inflation will by itself explain so large a discrepancy between the elastic resistance of normal and paralysed subjects.

The non-elastic resistance of the chest is that part of the resistance to inflation which is directly concerned with the rate of airflow in and out of the lungs. It is expressed in cm. water/litre/second, that is the number of cm. water pressure required to produce a flow of 1 litre/second. It is principally due to the resistance of the airways to the passage of air, though to a smaller extent, perhaps 20%, it is also the result of viscous resistance to changing the shape of the tissues. In paralysed tracheotomized patients the tracheotomy eliminates the resistance due to the upper

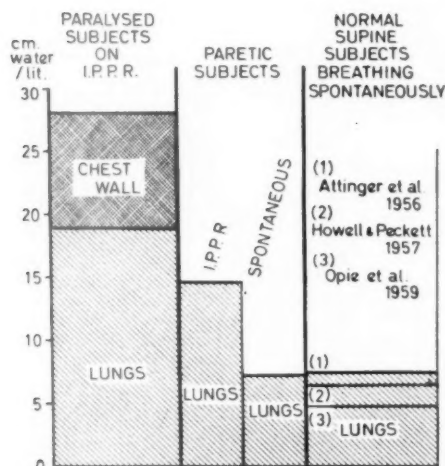


FIG. 2.—Elastic resistance of normal, paretic and paralysed subjects, all in the supine position.

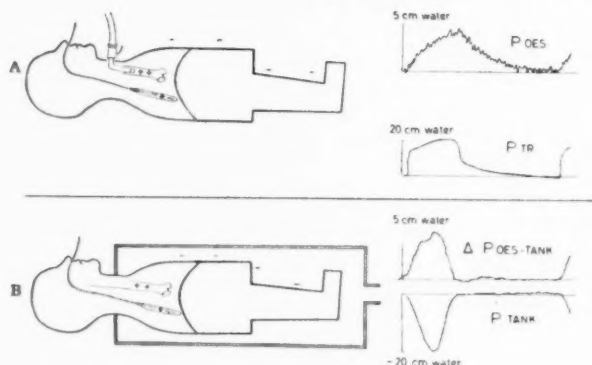


FIG. 3.—Relative pressure in trachea, œsophagus and on surface of the body during artificial respiration, A, by intermittent positive pressure respiration, and, B, in a tank respirator. Pressure tracings of œsophageal pressure (P_{OES}), tracheal pressure (P_{TR}), differential pressure between œsophageal and intra-tank pressures ($\Delta P_{OES-TANK}$), and intra-tank pressure (P_{TANK}) are shown.

airway—larynx, pharynx, nose and mouth—and introduces in its place resistance due to the tracheotomy tube, and we have been anxious to find out how this change balances out. The non-elastic resistance of the paralysed tracheotomized subject is similar to that of normal subjects but its constituent parts are very different (Opie *et al.*, 1959). The tracheotomy tube must, however, be large, preferably about 0.95 cm. bore (Magill, size 10), for the non-elastic resistance increases very steeply with smaller tubes, approximately varying inversely as the fourth power of the radius of the tube. The chest wall provides a small amount of viscous resistance. The lungs in paralysed patients, however, provide non-elastic resistance only about half that of normal supine subjects and this is surprising in view of the difficulty in keeping the airway of paralysed patients clear of secretions. The lower non-elastic resistance must be due to dilatation of the smaller bronchi either because they are distended by the raised pressure within them or because as the lungs are distended the bronchi themselves distend with them. It is possible both mechanisms are at work.

It is established that unless the chest is open, artificial respiration affects the circulation by impeding venous return to the right heart (Brecher, 1956). In intermittent positive pressure respiration, as gas is forced into the chest the intrathoracic pressure rises and therefore the pressure in mediastinum and right atrium may be higher than that in the peripheral veins which are themselves thin-walled structures exposed to atmospheric pressure (Fig. 3A). It is not always realized, however, that as far as the circulation is concerned the pressure relationships are exactly the same in artificial respiration in a tank respirator as in intermittent positive pressure respiration. During inspiration the pressure in the tank falls, the pressure in the trachea is nearly atmos-

pheric, considerably higher than the intra-tank pressure, and the mediastinal pressure is intermediate (Fig. 3B). It is clear therefore that in both types of artificial respiration the pressure during inspiration that is applied to the right atrium is higher than that to the peripheral veins, so that the venous return to the heart is impeded during inspiration.

Patients with diseases which necessitate artificial respiration are liable to circulatory disturbance, and it is of practical importance to know how this can be minimized. There are theoretical reasons for supposing that a high respiratory frequency with a low tidal volume is better for the circulation than a low respiratory frequency with a high tidal volume. We were anxious, however, to demonstrate whether this was so and to assess its importance.

Fig. 4 shows the expired minute volume in relation to the mean œsophageal pressure, the

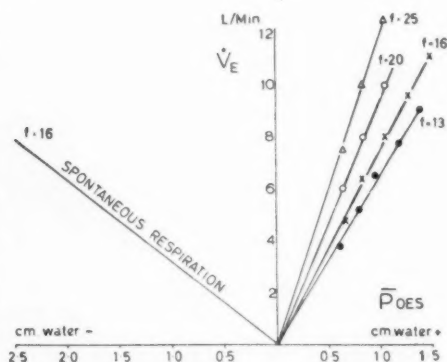


FIG. 4.—Relationship of mean œsophageal pressure (\bar{P}_{OES}) to expired minute volume (\dot{V}_E) during spontaneous respiration at frequency of 16/minute, and during intermittent positive pressure respiration at frequencies of 13, 16, 20 and 25/minute.

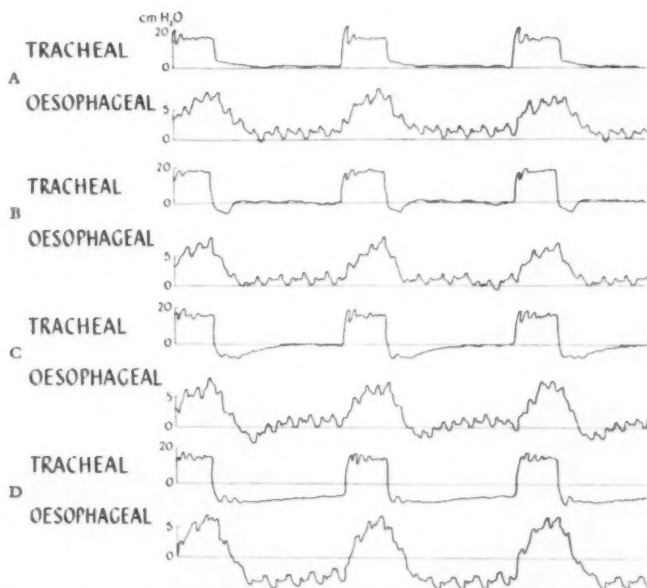


FIG. 5.—Tracheal and oesophageal pressures in intermittent positive pressure respiration with no negative pressure A, with brief negative pressure B and C, and with negative pressure throughout the period between inspirations D.

latter being used as an index of the obstruction to venous return. In a normal subject breathing spontaneously at a frequency of 16/minute and at a total ventilation of 8 litres/minute the mean oesophageal pressure is -2.5 cm. water. In patients on intermittent positive pressure respiration, at respiratory frequencies of 13, 16, 20 and 25 per minute the mean oesophageal pressure and therefore the obstruction to the venous return is less at higher than at lower frequencies. The difference, however, is relatively slight. At a total ventilation of 8 litres/minute the difference in mean oesophageal pressure between a normal subject and a patient on intermittent positive pressure respiration at a frequency of 13/minute is 3.25 cm. water. If the respiratory frequency is almost doubled to 25/minute the mean oesophageal pressure is only reduced by 0.5 cm. water. This is a relatively small effect.

A much more effective way of reducing the mean oesophageal pressure is by applying negative pressure in the expiratory phase. Fig. 5 shows records of tracheal pressure and oesophageal pressure in a paralysed patient receiving intermittent pressure respiration with no negative pressure (Fig. 5A), with a brief period of negative pressure (Fig. 5B and C), and with negative pressure of about 8 cm. water throughout the interval between inspirations (Fig. 5D). The

brief period of negative pressure quickens expiration, and the prolonged period of negative pressure strikingly reduces the oesophageal pressure so that the mean oesophageal pressure is close to that of a normally breathing person. If, however, the patient's bronchi are seriously weakened by chronic pulmonary disease, the negative pressure may cause the bronchi to collapse, trapping the air in the alveoli, so that the oesophageal pressure does not fall satisfactorily.

In conclusion I wish to stress that the kind of measurements here described not only have an intrinsic interest but are also of practical value in making it possible to understand what is happening to the patient, to assess the relative severity of the stresses to which he is subjected, and therefore the priorities in treatment.

REFERENCES

- ATTINGER, E. O., MONROE, R. G., and SEGAL, M. S. (1956) *J. clin. Invest.*, **35**, 904.
- BRECHER, G. A. (1956) *Venous Return*. London.
- HOWELL, J. B. L., and PECKETT, B. W. (1957) *J. Physiol.*, **136**, 1.
- OPIE, L. H., SPALDING, J. M. K., and STOTT, F. (1959) *Lancet*, **i**, 545.
- SPALDING, J. M. K., and SMITH, A. C. (1956) *Lancet*, **ii**, 1247.

DISCUSSION

Dr. Paul Forgacs (Dartford): When air is injected under the skin of the forearm, carbon dioxide diffuses into the surgical emphysema so created and reaches equilibrium with the partial pressure of this gas in the surrounding tissues within 80 minutes. Because of this relatively slow exchange, such a gas depot is less liable to short-term gains or losses of CO_2 than blood or alveolar gas. This technique is therefore applicable when the average level of the body's free carbon dioxide stores is to be measured.

In artificially ventilated patients a subcutaneous gas reservoir can be maintained for several days and sampled as often as necessary. The volume of ventilation is adjusted according to the concentration of CO_2 in the samples. Figures showing the correlation between subcutaneous CO_2 and the volume of ventilation were presented.

Dr. A. B. Kinnier Wilson (Hendon) said that at the Institute of Orthopaedics Poliomyelitis Centre they had had the same trouble with overventilation in chronic patients and had got over it by lengthening the tube between the valve (or bifurcation of the tubes) and the patient, thus restoring the upper half of the dead space (say 80 ml.). In one case, they had even increased this to a volume of 120 ml.; no ill-effects had been observed.

Dr. E. J. M. Campbell (London) warned against interpreting changes in elastic resistance in terms of changes of the physical properties of the lung tissue. He disagreed with Dr. Spalding if he said that "elastic resistance is nothing to do with

airflow". Elastic resistance and its reciprocal, compliance, depended upon distribution (Otis *et al.*, 1956).

He emphasized that changes in distribution both of ventilation and circulation were insufficiently considered during artificial ventilation and might account for many of the changes Dr. Spalding described. Thus they could cause the increase in elastic resistance. If so, then the elastic resistance would increase with increasing rates of breathing. Had this been observed?

He confirmed that in further studies Dr. J. B. L. Howell and he had found the rebreathing method for measuring pCO_2 very accurate, easy and clinically valuable (Campbell and Howell, 1959).

REFERENCES

- CAMPBELL, E. J. M., and HOWELL, J. B. L. (1959) To be published.
OTIS, A. B., MCKERROW, C. B., BARTLETT, R. A., MEAD, J., MCILROY, M. B., SELVERSTONE, N. J., and RADFORD, E. P. (1956) *J. appl. Physiol.*, **8**, 427.

Dr. Spalding replied that he had not intended to say that "elastic resistance had nothing to do with airflow", but to state that elastic resistance is measured when airflow has ceased. Dr. Campbell had argued that the frequency of respiration might affect the measurements obtained for elastic resistance. Dr. Spalding and his colleagues shared his anxiety about this as a possible source of error and therefore measured the elastic resistance while the patient was being inflated long enough for airflow to cease and for oesophageal pressure to remain stationary for a period of some seconds.

Meeting

April 3, 1959

Dr. P. HUGH-JONES (London) read a paper on *Assessing the Lungs*.

Meeting

May 1, 1959

Dr. DAVID BENAZON (London) read his Registrar's Prize Essay which was entitled *The Development and Clinical Use of Deep Hypothermia* (see *Lancet*, 1959, i, 745).

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Section of Urology

President—ALEC W. BADENOGH,
M.A., M.D., Ch.M., F.R.C.S.

Meeting
January 22, 1959

MEETING HELD AT ST. MARY'S WING OF

THE following cases were shown:

Four Cases of Functional Supernumerary Kidney
with Ectopic Ureter.

Three Cases of Advanced Bilateral Hydronephrosis,
due to Bladder Neck Obstructions.

Nephrectomy for Neoplasm of the Kidney, in
which a Portion of the Vena Cava was
Resected.

Painless Hæmaturia, due to Ureteric Calculus.

Painless Hæmaturia due to a Secondary Neoplasm
in the Kidney, as Presenting Symptom in
Carcinoma of Bronchus.

Intestinal Polyp Occurring at Site of Uretero-
colic Anastomosis.

Three Cases of Pyelitis Cystica.

Meeting
February 26, 1959

DISCUSSION ON PYELONEPHRITIS

Professor M. L. Rosenheim (London) opened the meeting by discussing some of the problems of pyelonephritis. Many of his views on the subject were previously published in the *Proceedings* (1954, 47, 628).

Dr. C. J. Hodson (London):

The Radiological Diagnosis of Pyelonephritis
Acute Pyelonephritis

Radiology has little to offer in the diagnosis of acute infections of the urinary tract. In some cases there appears to be increased tone in the renal pelvis and calyces whereas in others there appears to be a decreased tone. There may be slight overall increase in size of the affected kidney. The differentiation of these changes from normal variations is almost impossible in the individual case.

Chronic Pyelonephritis

The wide and somewhat varied use nowadays of the term "chronic pyelonephritis" necessitates some preliminary attempt at definition. For the sake of clarity and because of the somewhat practical nature of this contribution only the most commonly-occurring conditions are considered.

Characteristically the disease is in the nature of a coarse focal scarring often with areas of normal or hypertrophied renal tissue between, the line of demarcation between normal and

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Three Cases of Pelvi-ureteric Obstruction, Treated
by Renal Sympathectomy.

Two Cases of Ileal-loop Bladder for Contracted
Bladder.

Ileo-cystoplasty for Tuberculosis of Bladder.

A Single Kidney Functioning by Uretero-colic
Anastomosis, Performed by Mr. A. C.
Morson Twenty-two Years Ago.

Five Cases of Renal Cysts.

The following papers were read:

Renal Sympathectomy.—Mr. NEVILLE STIDOLPH.
The Treatment of Renal Injuries.—Mr. PETER
BOREHAM.

Ileal-loop Bladder for Contracted Bladder.—
Mr. PETER HARBISON.

Retroperitoneal Fibrosis.—Mr. JOHN GILLMAN.

abnormal being sharply defined. The kidney as a whole tends to be contracted and on its surface are coarse irregular depressions often associated with perirenal adhesions. The cut surface of such a kidney shows the normal architecture to be destroyed in the contracted regions, with a lack of differentiation between cortex and medulla, considerable fibrosis, and a blunting or complete absence of the associated renal papilla if the amount of tissue involved is large enough. This retraction of the renal papilla results in "caliectasis" or calycine "clubbing" which is recognizable on a radiograph.

It is this localized narrowing of the renal substance which gives rise to the cardinal radiographic sign of the disease and its demonstration depends on the focal lesions being large enough to give such an effect.

The form of the disease outlined above is not necessarily associated with other urinary abnormalities such as congenital malformation or the effects of urinary back pressure. It is the commonest manifestation of the disease in our experience, when there are no such complications. Its recognition therefore is the more important, as there may be nothing but its own features to suggest its presence.

Chronic infective changes are found also in

the renal pelvis, but these play little part in the matter of radiological recognition.

Chronic pyelonephritis, however, more commonly occurs not as a separate entity but as a complication of some other abnormality. Of these associated conditions by far the commonest is urinary obstruction, indeed it has been suggested that urinary stasis is a necessary precursor. It is not surprising therefore that pyelonephritic changes are often confused with those resulting from back-pressure and *vice versa*, indeed it may be impossible to separate the two. Moreover the pyelonephritic changes are often more diffusely scattered throughout the renal tissue in the back-pressure kidney and the characteristic coarse scarring may not be present.

The first radiological sign of back pressure in the kidney is dilatation of the pelvis or calyces or both, but occasionally calyceine dilatation is surprisingly slight in quite well-established cases. The next change is a blunting of the renal papillae due to atrophy of their substance. This in turn may be difficult to assess because of the wide normal variation. Later still the papillae are actually retracted, and marked "clubbing" of the calyces is seen on the pyelogram. Coincident with these changes in the papillae there is usually a demonstrable *generalized* narrowing of the renal substance due to atrophy, and there may be enlargement or reduction of the kidney size as a whole according to the amount of hydronephrosis.

The moderately advanced picture of back-pressure changes is thus of a uniform narrowing of kidney substance with equal clubbing of all the calyces and contrasts markedly with that due to the focal changes of chronic pyelonephritis.

Experience of these cases seems to suggest that chronic infective changes cannot in fact be diagnosed in the presence of back-pressure unless they produce added focal lesions of sufficient size further to contract the renal substance, and this is the stage at which our work now stands.

There is said to occur a diffuse form of chronic pyelonephritis in the absence of back-pressure. We have not yet encountered this type to our knowledge; it is thought to be very rare.

Many cases of recurrent urinary infection occur in which neither of these main disease entities develops to a recognizable degree. On the other hand (Staemmler and Dopheide, 1930), both can be present in an advanced form with very little in the way of symptomatology to indicate their presence. They may occur in almost any age group from infancy to old age, but tend to be more common in the first four decades of life and to occur more often in females.

Germane to this subject is the distinction made

by Kincaid-Smith (1955) between the renal changes arising from simple ischaemia and those caused by chronic pyelonephritis. In brief the macroscopic changes, with which we are presently concerned, in the ischaemic kidney are the result of a simple decrease in size of the kidney. This is a uniform change and its effect on the radiographic appearances will vary according to the size of the vessel affected. Thus in disease of the main renal artery the whole kidney is involved, whereas narrowing of one of its branches will cause a localized effect. Except in severe cases the cortex and medullary differentiation tends to be preserved, and there is characteristically an absence of clubbing of the calyces.

Excluding actual destruction of renal substance, for instance by tuberculous cavitation, there thus appear to be three causes for narrowing of renal tissue: fibrosis associated with infection, atrophy which is the result of back-pressure in the urinary tract, and atrophy or ischaemia which is the result of diminution in the blood supply.

RADIOLOGICAL DIAGNOSIS

In the normal kidney, whatever its shape or the distribution of its calyces, if a line be drawn through the tips of the outer renal papillae this line bears a constant relationship to the surface outline and the thickness of the renal substance can be measured arbitrarily as the distance between this line and the surface (Fig. 1). This thickness is usually increased but equal in the two polar regions and it varies considerably from case to case in the normal, depending on the size of the kidney and its morphological structure. It will obviously vary when the kidney is rotated about either its long or its horizontal axis but such rotation can usually be recognized from the pyelogram.

Analysis of 1,200 pyelograms has emphasized the remarkable degree of symmetry that is normally present between the two kidneys in any given individual both as regards their size, shape and pelvicalyceine pattern. This symmetry is also shared in the thickness of the renal substance and this provides the most useful practical yardstick for its measurement. When localized disease is present there is an upset between the relationship of the interpapillary line and the surface of the kidney, and variations in thickness of the renal substance can easily be detected (Fig. 2). In the case of extensive disease of focal character the whole structure may be so distorted that it is impossible to make out any normal pattern, nevertheless the clubbing of the calyces can still be distinguished and the narrowing of the renal substance can be made out (Fig. 3).

It will therefore be seen from the points outlined above that radiology provides a means

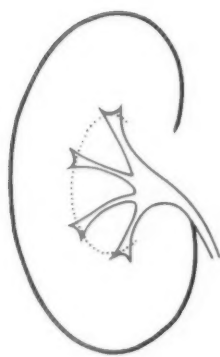


FIG. 1.

FIG. 1.—Diagram of the kidney showing interpapillary line used for measurement of thickness of renal substance.

FIG. 2.—M. B., female, aged 21. Tracing of excretory pyelogram. In two regions of the lower half of the right kidney there is localized narrowing of the renal substance and clubbing of the adjacent calyces. Early focal pyelonephritis.

FIG. 3.—E. S., female, aged 29. Tracing of excretory pyelogram. Advanced bilateral chronic pyelonephritis. Note small size of kidneys; irregular outlines; marked variations of the thickness of the renal substance with calyces clubbing.

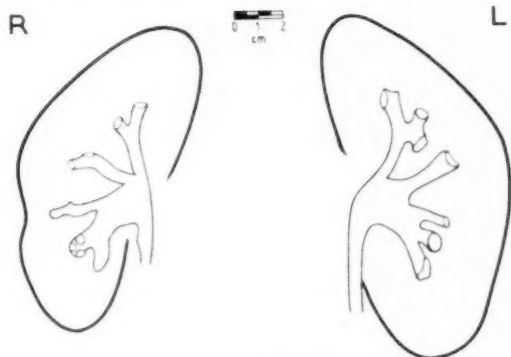


FIG. 2.

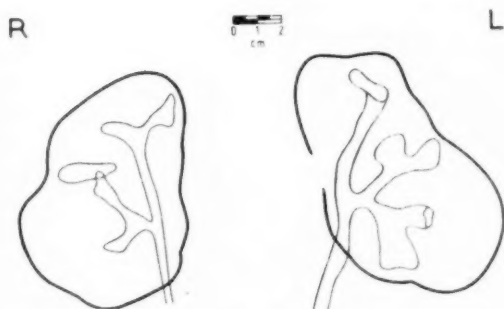


FIG. 3.

of assessing these coarse changes, provided both the renal outlines and the pattern of the renal pelvis, particularly of its calyces, can be defined. Failure to demonstrate the renal outline and incomplete filling of the renal pelvis and its calyces have been the main causes of incorrect diagnosis in these cases. On the other hand the precise definition of these details commonly presents a radiological problem which calls for every known technical ingenuity and quite often the use of such complicated procedures as tomography, perirenal gas insufflation and renal arteriography.

An analysis of 100 successive cases in which care had been taken to prepare the patient's abdomen before pyelography, and the radiographic factors adjusted to define the renal outlines, showed that such definition could be achieved in all but 6. The failures comprised chiefly old, bedridden people or infants. In the large majority of cases, therefore, the size of the kidneys can be measured during pyelography.

Modern contrast media also provide a means of adequate definition of the renal calyces during excretion pyelography, provided there is some preliminary dehydration of the patient and that effective ureteric compression is carried out.

Using 45% organic iodide medium we have found that in the absence of these ancillary measures we have had too high a failure rate of calyces definition. Recourse to retrograde pyelography does not always provide the answer, as this examination also calls for considerable skill to be effective. Indeed we have found that with care during excretion pyelography we can largely do without it.

However careful may be the attention to detail, cases will occur in which the renal outlines cannot be distinguished by the ordinary radiographic methods, usually because of overlying intestinal contents. One way out of this difficulty is to carry out tomography during excretion pyelography and we have found this of value in small children. There is, of course, an increased radiation risk inherent in this procedure but our experience is that only one or two tomographic "cuts" need be used, the rest of the child being protected from irradiation, and this may save repeated pyelographies. Indeed the seriousness of the lesion suspected is such that the risk due to this amount of radiation appears fully justified. Another technique is to opacify the kidneys by a rapid intravenous injection of a large quantity of opaque medium, for example 50 c.c. of 70%

organic iodide. A marked and prolonged "nephrogram" effect is obtained which enables accurate definition to be carried out. Another trick is to distend the stomach with gas by getting the patient to drink a "fizzy" drink, the gas-distended stomach pushing aside other overlying intestinal shadows in some cases. Another method with which we have not had much success is definition of the kidneys by means of retro-peritoneal gas insufflation. One of the difficulties is that the adhesions present in chronic pyelonephritis tend to prevent the gas coming into contact with the kidney.

At University College Hospital, after trying the simpler radiographic procedures, we now tend to pass straight on to renal arteriography. Not only does this give fine definition of the renal outlines but it also gives information with regard to the blood supply of both the suspected and normal kidneys, and we have found that by the amount and pattern of the opacification of the kidney during the nephrogram stage we have obtained valuable information as to vascularity. It has also provided a means of demonstrating unsuspected disease in the arterial supply to the apparently normal side in cases of unilateral disease.

The cases in which these advanced diagnostic techniques are used are, of course, those in which for some reason an accurate diagnosis requires to be made and in which other measures have failed. They comprise mainly young people suffering either from severe hypertension, or a long history of recurrent and debilitating urinary infection, in whom there seems a possibility that the disease may be unilateral and in whom nephrectomy is being considered. We have found arteriography in particular to be of the utmost value in such cases.

The most striking radiographic finding commonly associated with chronic pyelonephritis is the reduced size of the affected kidney compared with the opposite side when the disease is unilateral. This reduction is a true overall diminution in size but is accentuated by the accompanying hypertrophy of the opposite kidney if this is normal. Such hypertrophy is, or should be, a constant finding where a large amount of renal tissue is destroyed on the affected side. We regard it as a very reassuring sign if nephrectomy is to be contemplated, and we view with considerable suspicion "sound" kidneys which are not of a normal or above-normal size. Another feature which is commonly found is the production of a high concentration of opaque medium in the urine of the affected kidneys. Even when severe structural changes are present and the kidney is very small and deformed there may be a surprisingly high con-

centration. In the case of unilateral disease we have frequently noted, when arteriography has been carried out, that the renal artery to the affected side is greatly reduced in diameter compared with the normal. And, as mentioned above, in the nephrographic stage of renal arteriography we have been able to demonstrate a remarkably constant association between the vascularity of the kidneys and the structural changes found in the specimen after nephrectomy.

DIFFERENTIAL DIAGNOSIS

The main problems of differentiation from the radiological point of view have been provided by renal tuberculosis, infarction, papillary necrosis and a simple back-pressure effect without infection.

Tuberculosis can usually be excluded by urine culture. Our experience in the case of infarcts is that as a rule clubbing of the calyces is slight or absent, and we use this as an important point between ischaemic atrophy and the contraction due to fibrosis. With the rare papillary necrosis differentiation may be difficult, but here again there is usually no associated depression of the renal surface opposite the clubbed calyx. The back-pressure effects of lower urinary obstruction provide one of the main problems. Our experience suggests that it is impossible radiologically to define a chronic infective change superimposed on a back-pressure kidney unless the result of infection is focal in nature. Certainly shrinkage of the kidney with a generalised narrowing of its substance and clubbing of the calyces is not a sign of pyelonephritis, and in two kidneys removed at operation where these radiological changes were present, there has been no sign of an infective change in the operative specimen.

There is one more category of chronic renal disease which has, in our experience, added confusion. This is the small, often irregular, kidney in which there is clubbing of the calyces and dilatation of the whole or part of the ureter, but in which there is no apparent obstruction to the flow of urine as demonstrated by pyelography. We believe that among the group of kidneys showing these characteristics will be found a high proportion in which reflux occurs up the ureter during micturition.

To sum up, therefore, the radiological diagnosis of chronic pyelonephritis is mainly based on the focal form of this disease and depends on the demonstration of localised contraction of the renal substance associated with clubbing of the adjacent calyx.

REFERENCES

- KINCAID-SMITH, P. (1955) *Lancet*, ii, 1263.
STAEMMLER, M., and DOPHEIDE, W. (1930) *Virchow's Arch.*, 277, 713.

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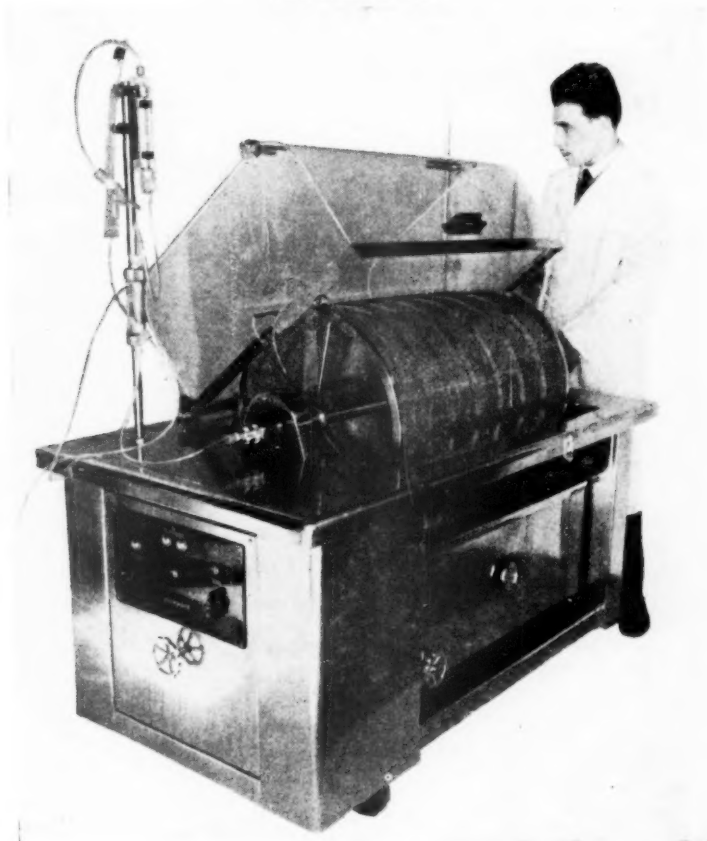
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ARTIFICIAL KIDNEY

NECKER MODEL



References

PARIS: Hopital Necker, Hopital Militaire du Val-de-Grace, Hopital Foch.
Centres Hospitaliers Regionaux de Bordeaux, Dijon, Lyon, Marseille, Montpellier, Nancy.
GREAT BRITAIN: Postgraduate Medical School of London, Hammersmith Hospital,
London; Glasgow Royal Infirmary, Glasgow.
Centre Hospitalier de Bucarest (Rumania), de Lisbonne (Portugal), Clinique Universitaire de
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Section of Comparative Medicine

President—F. O. MACCALLUM, M.D.

Meeting

February 18, 1959

A DISCUSSION was held on **Respiratory Virus Infections of Man and Animals**; opening papers were read as follows:

Relationships between Influenza Viruses of Animal and Human Origin.—Dr. C. H. ANDREWES and Miss G. WORTHINGTON.

Viruses and Pleuropneumonia-like Organisms in

Meeting

March 18, 1959

HELD AT THE CHESTER BEATTY RESEARCH INSTITUTE, INSTITUTE OF CANCER RESEARCH:
ROYAL CANCER HOSPITAL

THE following demonstrations were given:

BIOLOGICAL ALKYLATING AGENTS

Cyto-active Amino Acids and Peptides.—F. BERGEL, J. A. STOCK and R. WADE. See Bergel, F., and Stock, J. A. (1959) *J. chem. Soc.*, p. 97; Bergel, F., and Wade, R. (1959) *J. chem. Soc.*, p. 941.

A Rapid Biochemical Effect Produced by Nitrogen Mustards.—A. R. CRATHORN and G. D. HUNTER.

Recent Work on Potential Growth Inhibitors.—W. DAVIS, J. J. ROBERTS, W. C. J. ROSS, G. P. WARWICK, J. WILSON and T. A. CONNORS. See Roberts, J. J., and Warwick, G. P. (1957) *Nature, Lond.*, **179**, 1181; (1958) *Biochem. Pharmacol.*, **1**, 60. Ross, W. J. C., and Davis, W. (1957) *J. chem. Soc.*, p. 2420.

Mutagenicity of the Alkylating Carcinogens.—O. G. FAHMY and M. J. FAHMY. See Fahmy, O. G., and Fahmy, M. J. (1957) *J. Genet.*, **55**, 280; (1958) *Ann. N.Y. Acad. Sci.*, **68**, 736.

The Action of Alkylating Agents Studied in *E. coli*-bacteriophage Systems.—A. LOVELESS and J. STOCK. See Loveless, A. (1958) *Nature, Lond.*, **181**, 1212.

CANCER OF URINARY BLADDER

The Metabolism of 2-Naphthylamine.—E. BOYLAND and D. MANSON. See Boyland, E., and Manson, D. (1958) *Biochem. J.*, **69**, 601.

AUGUST

Respiratory Diseases of Poultry.—Dr. H. P. CHU. See Chu, H. P. (1958) *Vet. Rec.*, **70**, 55, 1064.

Respiratory Virus Diseases and Respiratory Diseases of Supposed Virus Aetiology in Pigs.—Dr. P. WHITTLESTONE. See Whittlestone, P. (1957) *Vet. Rec.*, **69**, 1354; Whittlestone, P. (1958) *Enzootic Pneumonia of Pigs and Related Conditions*, Ph.D. Thesis Cambridge.

β -Glucuronidase Activity of the Urine.—E. BOYLAND, D. M. WALLACE and D. C. WILLIAMS. See Boyland, E., Wallace, D. M., and Williams, D. C. (1957) *Brit. J. Cancer*, **11**, 578.

Enzymic Hydrolysis of Metabolites of Carcinogenic Aromatic Amines.—E. BOYLAND and K. WILLIAMS.

Chromatography of Urinary Extracts with Reference to the Metabolism of Tryptophan.—D. C. WILLIAMS. See Boyland, E., and Williams, D. C. (1956) *Biochem. J.*, **64**, 578.

CHEMOTHERAPY

Tumour-inhibitory Styryl Compounds.—S. S. BROWN, C. L. LEESE, J. H. LISTER and G. M. TIMMIS.

Tumour-inhibiting Amino Acids.—T. A. CONNORS and W. C. J. ROSS. See Connors, T. A., Elson, L. A., and Ross, W. C. J. (1958) *Biochem. Pharmacol.*, **1**, 239; Connors, T. A., and Ross, W. C. J. (1958) *Biochem. Pharmacol.*, **1**, 93.

Hematological Effects of Cytostatic and Anti-leukæmic Agents.—L. A. ELSON. See Elson, L. A. (1958) *Ann. N.Y. Acad. Sci.*, **68**, 826; Elson, L. A., Galton, D. A. G., and Till, M. (1958) *Brit. J. Haemat.*, **4**, 355.

CYTOLOGY

Tumour Karyology.—P. C. KOLLER and A. J. S. DAVIES.

ENZYMES AND CO-ENZYMES IN CANCER RESEARCH

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Carcinogenesis by Cholesterol and its Derivatives.—I. HIEGER. See Hieger, I. (1958) *Brit. med. Bull.*, **14**, 159.

The Modes of Action in Carcinogenesis by Plastic Films.—E. S. HORNING. See Alexander, P., and Horning, E. S. (1959) In: Wolstenholme, G. E. W., and O'Connor, M., eds. Ciba Foundation Symposium on Carcinogenesis: Mechanics of Action. London; p. 12.

The Influence of Hormones on the Induction of Cutaneous Melanomas by Carcinogenic Hydrocarbons in the Syrian Hamster.—E. S. HORNING. See Horning, E. S. (1956) *Brit. J. Cancer*, **10**, 678; (1958) *Ciba Found. Coll. Endocrin.*, **12**, 22.

An Oestrogen/Androgen-induced Tumour of the Flank Organ in the Syrian Hamster.—HADLEY KIRKMAN.

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Enzymic Hydroxylation of Aromatic Compounds by Liver Microsomes.—J. BOOTH and E. BOYLAND. See Booth, J., and Boyland, E. (1957) *Biochem. J.*, **66**, 73; (1958) *Biochem. J.*, **70**, 681.

Synthetic Studies Related to Purine Metabolism.—S. S. BROWN, C. L. LEESE, J. H. LISTER and G. M. TIMMIS. See Leese, C. L., and Timmis, G. M. (1958) *J. chem. Soc.*, pp. 4104, 4107.

Metabolism of Liver Cytoplasm.—E. REID, C. J. SMITH and J. T. NODES. See Reid, E. (1958) *Brit. J. Cancer*, **12**, 428. Reid, E., and Stevens, B. (1958) *Nature, Lond.*, **182**, 441; (1958) *Biochem. J.*, **68**, 367.

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Studies of Tumour Cells by Ultraviolet, Fluorescence and Interference Microscopy.—R. J. KING and E. M. F. ROE. See King, R. J., and Roe, E. M. F. (1958) *J. R. micr. Soc.*, **76**, 168.

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Protein Synthesis in *B. megaterium*.—J. A. V. BUTLER, A. R. CRATHORN and G. D. HUNTER. See Butler, J. A. V., Crathorn, A. R., and Hunter, G. D. (1958) *Biochem. J.*, **69**, 544.

Demonstrations of the Heterogeneity of DNA from Human Tissues and other Sources.—J. A. V. BUTLER and K. V. SHOOTER. See Butler, J. A. V., and Shooter, K. V. (1958) *Z. phys. Chem.*, **15**, 6.

Effects of Ionizing Radiations on DNA and its Constituent Nucleotides.—G. HEMS.

Effects of Alkylating Agents on DNA and its Constituent Nucleotides.—P. D. LAWLEY. See Lawley, P. D. (1956) *Biochim. biophys. Acta*, **22**, 451; (1957) *Biochim. biophys. Acta*, **26**, 450.

Methods of Fractionating and Characterizing Histones.—D. M. P. PHILLIPS and E. W. JOHNS. See Phillips, D. M. P. (1958) *Biochem. J.*, **68**, 35.

Effects of Non-ionizing Radiations on DNA and its Constituent Nucleotides.—C. REINER and E. M. F. ROE.

Effects of Ionizing Radiations on Nucleic Acids and Nucleoproteins.—K. A. STACEY and P. ALEXANDER. See Alexander, P., and Stacey, K. A. (1958) *Ann. N.Y. Acad. Sci.*, **68**, 1225.

Changes Produced by Nitrogen Mustards and Related Compounds in the Structure of Nucleic Acids and Nucleoproteins.—K. A. STACEY, J. T. LETT and P. ALEXANDER. See Alexander, P., and Stacey, K. A. (1958) *Ann. N.Y. Acad. Sci.*, **68**, 1225; Stacey, K. A., Cobb, M., Cousens, S. F., and Alexander, P. (1958) *Ann. N.Y. Acad. Sci.*, **68**, 682.

PROPERTIES OF THE CELL SURFACE

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Specific Reactions of Polymers with the Surfaces of Tissue Cells.—E. J. AMBROSE, D. M. EASTY and P. C. T. JONES. See Ambrose, E. J., Easty, D. M., and Jones, P. C. T. (1958) *Brit. J. Cancer*, **12**, 439.

The Chemical Groups Associated with the Surface of Tumour Cells. Serological Studies of the Specificity of the Cell Surface.—G. C. EASTY, D. M. EASTY and E. J. AMBROSE.

Electrophoretic Studies of the Differences between Normal and Tumour Cells.—J. H. B. LOWICK and A. M. JAMES (Chelsea College of Science), G. KLEIN (Karolinska Institutet, Stockholm), L. PURDOM and E. J. AMBROSE. See Purdom, L., Ambrose, E. J., and Klein, G. (1958) *Nature, Lond.*, **181**, 1586.

Influence of Strong Electrostatic Fields on the Growth of Certain Fungi.—D. ROSEN.

PUBLICATIONS

- (1) Works from the Thurstan Holland Collection of Radiological Literature. (2) The Institute Library. (3) Staff Publications Illustrating the Pathways of Cancer Research.—D. A. BRUNNING and M. AMOSU.

RADIOBIOLOGY

- Shortening of Life Span ("Accelerated Ageing") by Radiations and Mutagenic Chemicals.—D. I. CONNELL.

- The Relation Between X-ray Dose and Yield of Chromosome Aberrations.—S. H. REVELL. See Revell, S. H. (1958) *Ann. N. Y. Acad. Sci.*, 68, 802.

SPECTROSCOPY

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- Physico-chemical Investigations of Tumour-

- inhibitory Styrylquinoline and Stilbene Derivatives.—R. LUMLEY JONES, P. D. LAWLEY and E. M. F. ROE.

TECHNICAL APPLICATIONS

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- Histological Preparations of Fragments of Aspirated Human Bone Marrow.—D. A. G. GALTON and E. WOOLLARD.

- Applications of Photography in Cancer Research.—K. G. MOREMAN.

Meeting
April 15, 1959

DISCUSSION ON ADAPTATIONS OF MAN AND ANIMALS TO THEIR ENVIRONMENT

Dr. P. R. Lewis (Cambridge):

Adaptation of Man to a Change in Day Length

Most animals, including man, exhibit a diurnal cycle of rest and activity; and most of their bodily processes show a parallel twenty-four-hour rhythm. It is now known that the diurnal rhythm in many of these processes will persist for long periods of time under environmental conditions which are either kept constant or made to vary with an abnormal periodicity (for a recent review covering the whole animal kingdom, see Harker, 1958). In order to study the persistence of diurnal rhythms in man, expeditions to Spitzbergen were organized from Cambridge in the summers of 1953 and 1955. On these expeditions groups of subjects lived for about six weeks as isolated communities on a rigidly controlled *day* of an abnormal length. In all, 8 subjects lived on a twenty-two-hour *day*, 7 on a twenty-one-hour and 5 on a twenty-seven-hour *day*. During the summer months in Spitzbergen light intensity and temperature vary so little that the main rhythm in the environment was that imposed by the subjects themselves and this was rigidly controlled by wrist watches and alarm clocks which had been specially adjusted to indicate the appropriate experimental time scale. Various diurnal rhythms were studied, attention being concentrated on those which earlier work had shown to be particularly persistent. The detailed results of these experiments have already been published (Lewis *et al.*, 1956; Lewis and Lobban, 1956, 1957); and the present paper deals specifically with their

relevance to the problem of adaptation to days of abnormal length.

The results obtained on the three abnormal time scales were sufficiently similar for them to be considered together. Considering first the excretory rhythms, only four of the subjects adapted immediately to the new routine; that is, the majority of subjects had excretory rhythms with a marked twenty-four-hour periodicity for at least the first week on an abnormal time routine. During subsequent weeks, however, this twenty-four-hour component of the excretory rhythm gradually disappeared in a number of the initially-unadapted subjects. In some, however, there was still a significant twenty-four-hour component at the end of the period on the abnormal routine. There is thus considerable individual variation in the response, both initially and subsequently. In spite of the small number of subjects studied it seems reasonable to conclude that rapid initial adaptation to an abnormal time routine is relatively uncommon, that most people will slowly adapt over a period of a few weeks, but that a small proportion may take many weeks, or even months, to become fully adapted. One striking result obtained in 1955 was that two subjects who were initially well adapted showed only poor adaptation after a prolonged sledging trip (Lewis and Lobban, 1958). Though the data are for two subjects only, it is more than likely that severe physical exertion (and possibly other forms of "stress" too) reduces a person's ability to adapt to an abnormal time routine.

In any one individual not all the diurnal rhythms adapt at the same rate. Thus the rhythm of body temperature became adapted to the environmental time scale in most of our subjects within a few days, though there is evidence for a persistent twenty-four-hour rhythm of body temperature in some subjects (Kleitman and Kleitman, 1953). There is even a marked difference in response in the various excretory rhythms. Thus that of phosphate studied by Mills and Stanbury (1952) adapts very rapidly. Of the excretory rhythms studied in Spitzbergen, that of potassium definitely had a more persistent twenty-four-hour component than those of sodium, chloride and water. Hence adaptation to an abnormal time scale is in most subjects a complex process, first one and then another of the physiological mechanisms becoming adjusted to the new environment.

One is tempted to speculate on the possible mechanism responsible for the persistent twenty-four-hour rhythm. The hypothalamus may be the site of the "clock" mechanism for it is in this region of the diencephalon that centres appear to exist for the control of body temperature, water balance and aldosterone output. It may be that groups of neurons concerned with the control of a particular autonomic function become so conditioned by the rhythmic nature of afferent impulses that they continue to respond with the old twenty-four-hour rhythmicity for some time after the pattern of afferent information has been changed.

REFERENCES

- HARKER, J. E. (1958) *Biol. Rev.*, **33**, 1.
 KLEITMAN, N., and KLEITMAN, E. (1953) *J. appl. Physiol.*, **6**, 283.
 LEWIS, P. R., and LOBBAN, M. C. (1956) *J. Physiol.*, **133**, 670.
 ———, ——— (1957) *Quart. J. exp. Physiol.*, **42**, 356, 371.
 ———, ——— (1958) *J. Physiol.*, **143**, 8P.
 ———, ———, and SHAW, T. I. (1956) *J. Physiol.*, **133**, 659.
 MILLS, J. N., and STANBURY, S. W. (1952) *J. Physiol.*, **117**, 22.

Dr. J. D. Findlay (Ayr):

Some Adaptations of Farm Animals to Climatic Stress

The adaptation of farm animals to climate has attracted the interest of many physiologists and has been the subject of much speculation in recent years. With the development of climatic chambers capable of housing large farm animals much former speculation on the subject has been shown to have a factual basis. This paper

deals broadly with some aspects of adaptation in farm animals in general but with cattle in particular since it is with the latter that most recent work has been concerned.

The morphology of farm animals is related to the climate in which they live. Bergman's and Allen's "rules" or generalizations (Bergman, 1847; Allen, 1877) suggest that warm-blooded species in cold climates tend to be larger than comparable species in tropical climates while there is a general tendency for enlargement of the peripheral parts in the tropics. Increased surface area to body weight ratio tends to increase the efficiency of heat dissipation. The nature and extent of the body covering in actual physical contact with the environment is also a factor of importance in determining animal adaptation. In 1854 Wilson noted that in cold countries animals tended towards the fleecy coat of the sheep whereas in warm countries hair was strongly developed and wool almost totally absent. Any discussion, however, of the morphological adaptations of farm animals must consider also the indirect effect of climate on body conformation. This indirect effect, largely due to the influence of rainfall on vegetation, affects the size, conformation, grazing habits and range of farm animals as well as the structural formation of their digestive tracts. The nature of the terrain also affects the development of specialized structural adaptations. These indirect effects of climate must be considered when speculating, for example, on the almost universal phenomenon of the dwarfing of cattle in the hot-wet tropics or the concentration of fat in the hump of the camel or in the tail or rump of desert sheep which is analogous to the steatopygia of the Hottentot. Lastly, in considering structural adaptations to climate the symbiotic relationship of farm animals to man must be borne in mind. Thus, their climatic environment is altered by housing, their supply of fodder is regularized and the external conformation of the animals much altered by specialized breeding.

With these provisos clearly stated the relation between the gross conformation of farm animals and climate is very striking as Wright (1954) has admirably shown. Thus, the yak from the cold plateaux of Central Asia has a heavy and compact body, short legs and neck, small dewlap, short tail and ears and is heavily haired. These characteristics are apparent in less exaggerated form in cattle of cool temperate zones, e.g. in Highland cattle. In contrast, subtropical cattle of the warm temperate zone have rangier frames and larger extremities and, most markedly, an increase in dewlap area.

This latter characteristic is exaggerated in the zebu cattle of the dry tropics. There are folds of corrugated skin from the sheath to the scrotum, and the vulva is much corrugated. Certain breeds of zebu, e.g. the Gir, have very large and pendulous ears offering greatly increased surface area for heat loss. The nature of the body covering is changed from the thick, dull coat of northerly cattle to the short, fine-haired coat of high sheen characteristic of tropical cattle. The almost universal prevalence of dwarfed cattle in the hot-wet tropics suggests a relation between size and climatic adaptation, though the suggestion, in view of what has been stated previously, must be treated with reserve.

Sheep and goats exhibit similar changes in conformation which could be speculatively ascribed to climatic adaptation. The Romney Marsh sheep with their thick and compact body conformation and coats, stocky legs and small ears are in marked contrast to the southern desert sheep which exhibit extraordinarily long extremities and which are covered with very short and fine hairs comparable in texture to the hairs of zebu cattle. Similar differences exist in goats.

It is, however, in the behaviour and physiological reactions of cattle to climatic stress that adaptative mechanisms can be most clearly demonstrated. The heat balance of the animal can be maintained only by alterations in heat production or in heat loss.

Gross differences in the adaptability of cattle to climatic stress are readily seen in studies of their grazing behaviour since voluntary limitation of food intake as a means of decreasing heat production is a primary adaptative mechanism in cattle. Two examples from many reviewed by Findlay (1950) will serve as illustrations. Thus, when Aberdeen-Angus and Brahman cattle were exposed to a climate of sun and no wind at an air temperature around 32° C. the Aberdeen-Angus spent 54% of its time in grazing and rested only in the shade whereas the Brahman grazed for 71% of its time and rested only in the sun. Under the same conditions but on windy days the grazing time of the Aberdeen-Angus increased to 75% but it still rested only in the shade (Rhoad, 1938). Jersey and Holstein cattle at 28° C. spent only 11% of their time grazing but at night at the same temperature they spent 37% of their time in grazing since they had not to contend with the added burden of solar radiation (Seath and Millar, 1946). Friesian cows exported to Fiji have been observed to graze mainly at night and to spend most of the day lying down (Payne *et al.*, 1951). Such behavioural studies indicate that cattle primarily

adapt themselves to heat stress by reducing their food intake and this is amply confirmed in climatic chamber studies. Thus, Worstell and Brody (1953) have shown that air temperatures above 27° C. cause a rapid depression in food intake in European breeds of cattle which cease feeding altogether at 41° C. These changes bring about depression of heat production and this depression has been shown to occur in European-type cattle at above 27° C.

Resulting from the decrease in food consumption in cattle the milk yield declines and this occurs around 27° C. in European-type cows (Cobble and Herman, 1951). These changes are associated with changes in the milk and blood composition. For example, the levels of fat and chloride in the milk increase while those of lactose, total nitrogen and total solids-not-fat decrease. Blood creatinine increases with increasing rectal temperature, reflecting the accelerated endogenous nitrogen catabolism following the decline in food consumption (Worstell and Brody, 1953).

Unlike man, cattle exposed to thermal stress do not show disturbances in their electrolyte or water balance or in the protein concentration in their blood. Short exposures of dairy calves to very severe heat stress produce transient haemoconcentration but this is due more to mobilization of erythrocytes than to loss of water from the blood. During such exposures blood and plasma volumes tend to increase (Bianca, 1957).

The most profound differences between cattle and man when adapting themselves to thermal stress lie in their cardio-respiratory behaviour and skin function. European-type cattle exhibit a sudden acceleration in outer surface vaporization at air temperatures around 16° C. and this acceleration declines around 24° C. with a consequent rise in rectal temperature to the almost lethal level of 42° C. at an air temperature of 41° C. In cattle at 41° C. air temperature the ratio of evaporative heat loss to total heat production is about half that of the corresponding ratio for man (Worstell and Brody, 1953). Vasodilatation is almost maximal in the calf at 20° C. air temperature (Beakley and Findlay, 1955a) and heart-rate increases only slightly with increasing thermal stress (Beakley and Findlay, 1955b).

These differences in outer surface vaporization are partly accounted for by the fact that the sweat glands of cattle are apocrine, with a relatively poor blood supply, secreting a mucopolysaccharide (Findlay and Yang, 1950; Yang, 1952). There is no doubt, however, that these sweat glands are active (Dowling, 1958) though

there is as yet no evidence that the process of adaptation to heat stress in European cattle involves increases in the functional efficiency of their sweat glands. Part of the superiority of zebu cattle in hot climates has been attributed to more efficient sweating (Klemm and Robinson, 1955).

One of the most striking differences between man and cattle in their adaptation to thermal stress is to be found in the respiratory activity of cattle. Panting in cattle is very roughly the equivalent of profuse sweating in man so far as adaptation to climatic stress is concerned. Cattle subjected to climatic stress can attain respiratory frequencies as high as 250/min. compared with a normal value of about 60/min. The rate of ventilation increases almost linearly with temperature. The increase of ventilation rate is initially maintained by increasing the frequency and diminishing the tidal volume until at an upper critical rectal temperature of 40.5° C., when the frequency is maximal, tidal volume increases, the frequency is consequently reduced, overventilation occurs, the heart-rate is suddenly increased and the animal develops a severe respiratory alkalosis (Findlay, 1957; Bianca, 1955; Bianca, 1958; Dale and Brody, 1952). Acclimatization of cattle to heat stress is characterized by progressive reductions in the magnitude of the frequency of respiration and by the establishment of true panting, i.e. high frequency, low tidal volume breathing (Bianca, 1959).

The influence of the coat cover on the adaptation of farm animals to climatic stress has been clearly demonstrated by Blaxter and his colleagues (Armstrong *et al.*, 1959). They demonstrated that on maintenance levels of feeding the critical temperatures of a sheep with 0.1 cm., 2.5 cm. and 12 cm. fleece lengths were 32° C., 13° C. and 0° C. respectively. A heavy fleece not only depresses the critical temperature but also reduces the rate of increase of heat loss with falling temperature under subtropical conditions.

The colour and quality of the coat affects the adaptation of cattle to climatic stress by its influence as a reflector of radiant energy and as an insulating medium. White Zulu cattle absorb some 49% of incident solar radiation on their hides compared with 89% by black Aberdeen-Angus cattle while dull, woolly-coated cattle have been shown to have much less heat tolerance than glossy-coated cattle of the same breed, due largely to the high insulation of the woolly coat (Findlay, 1954). Bianca (1959) has shown that clipping the coat of calves greatly enhances their ability to withstand very severe thermal stress.

The distribution of body fat also affords an

example of climatic adaptation. Thus it has been shown that European-type cattle tend to lay down fat subcutaneously whereas tropical cattle tend to have the fat distributed intramuscularly with a consequent advantage in heat dissipation (Payne and Ledger, 1959).

Adaptation of farm animals to cold consists principally in growth of the haired coat and little work has been done on this aspect.

Briefly, cattle and sheep adapt themselves to climatic heat stress by reducing food intake, by coat shedding, by increasing the efficiency of evaporative loss by respiratory activity, and to a slight extent by increasing the efficiency of outer surface vaporization of moisture. The mechanisms involved in the adaptation of farm animals to climatic stress are, however, still very imperfectly understood.

REFERENCES

- ALLEN, J. A. (1877) *Radical Rev.*, **1**, 108.
 ARMSTRONG, D. G., BLAXTER, K. L., GRAHAM, N. McC., and WAINMAN, F. W. (1959) *Anim. Prod.*, **1**, 1.
 BEAKLEY, W. R., and FINDLAY, J. D. (1955a) *J. agric. Sci.*, **45**, 373.
 ———, ——— (1955b) *J. agric. Sci.*, **45**, 461.
 BERGMAN, A. (1847) *Göttingen Studien*, **1**, 595.
 BIANCA, W. (1955) *J. agric. Sci.*, **45**, 428.
 ——— (1957) *Brit. vet. J.*, **113**, 227.
 ——— (1958) *J. agric. Sci.*, **51**, 321.
 ——— (1959) *J. agric. Sci.*, **52**, 380.
 COBBLE, J. W., and HERMAN, H. A. (1951) *Res. Bull. Mo. agric. Exp. Sta.*, No. 485.
 DALE, H. E., and BRODY, S. (1952) *J. Anim. Sci.*, **11**, 790.
 DOWLING, D. F. (1958) *Austr. J. agric. Res.*, **9**, 579.
 FINDLAY, J. D. (1950) *Bull. Hannah Dairy Inst.*, No. 9.
 ——— (1954) *Progress in the Physiology of Farm Animals*. London; **1**, 252.
 ——— (1957) *J. Physiol.*, **136**, 300.
 ———, and YANG, S. H. (1950) *J. agric. Sci.*, **40**, 125.
 KLEMM, G. H., and ROBINSON, K. W. (1955) *Austr. J. agric. Res.*, **6**, 350.
 PAYNE, W. J. A., LAING, W. L., and RAIVOKA, E. N. (1951) *Nature, Lond.*, **167**, 610.
 ———, and LEDGER, T. (1959) *Nature, Lond.* (In press.)
 RHOAD, A. O. (1938) *Proc. Amer. Soc. Anim. Prod.*, Nov., p. 284.
 SEATH, D. M., and MILLAR, G. D. (1946) *J. Dairy Sci.*, **29**, 199.
 WILSON, J. M. (1854) *The Rural Cyclopaedia*. Edinburgh; p. 577.
 WORSTELL, D. M., and BRODY, S. (1953) *Res. Bull. Mo. agric. Exp. Sta.*, No. 515.
 WRIGHT, N. C. (1954) *Progress in the Physiology of Farm Animals*. London; **1**, 191.
 YANG, S. H. (1952) *J. agric. Sci.*, **42**, 465.

Dr. O. G. Edholm (London):

The adaptation of man to climatic stress has been extensively studied. There is unequivocal evidence of physiological adaptation to heat. These changes include an increased sweat-rate, a diminished rise in body temperature and in pulse-rate, and an increased sense of well-being during work in the heat. Such changes are demonstrable after a few days' exposure to a hot environment and appear to be fully developed after fourteen days. There is evidence that the blood volume increases during this period and there is a diminished excretion of sodium chloride in the sweat owing to increased activity of the adrenocortical hormones. These changes can also be produced by exposing men daily in a hot room for periods of four hours a day only. So men can be artificially acclimatized to heat in this country, although for twenty out of the twenty-four hours of the day they are not exposed to heat stress at all. Such artificial acclimatization appears to resemble natural acclimatization acquired by living in a hot country, and so far no significant difference has been demonstrated between natural and artificial acclimatization.

On the other hand, in spite of very considerable investigation, there is as yet only scanty evidence of acclimatization of men to cold. This is in striking contrast to studies of laboratory animals, including rats, mice, guinea-pigs and rabbits, all of which have been successfully acclimatized to severe cold. Such acclimatized animals will survive at temperatures at which non-acclimatized litter mates will die. This acclimatization is achieved by increased heat production, and it is probable that the heat production is due to an increased metabolic rate in other than muscle tissue. There is also evidence of changes in the

enzyme systems of the liver and other organs.

Wild animals living in the Arctic achieve their adaptation to severe cold not by an increased metabolic rate but by a very efficient insulation. This insulation is provided by fur and to a certain extent by the thickness of subcutaneous fat. Laboratory experiments on men in climatic chambers have on the whole been disappointing, and such changes which have been described have been small possibly because the length of time for which subjects could be exposed to cold is too short. There have been many studies in the field, particularly in recent years on polar expeditions, and there have also been studies of people living permanently in the cold, including the Eskimo and the Australian aborigine. Food intake is considerable amongst polar explorers, but studies of the energy intake in Eskimos suggest that their levels of calorie consumption are similar to those in temperate countries.

Basal metabolic rate has been measured in the Eskimo and most studies have demonstrated an increase of the order of 15–20%. This has, however, been attributed to the high protein intake of the Eskimo. There does not appear to be any increase in the basal metabolic rate in men spending up to two years in polar regions. There is good evidence of local acclimatization to cold in the fingers and there are many observations suggesting subjective adaptation, in that the sensation of cold is diminished after prolonged exposure and less clothing is required to meet particular cold stress.

Man has been termed a tropical animal and his adaptation to cold appears to be to learn how to live at low temperatures—that is, man has to rely on clothes and shelter and skill rather than physiological adjustment.

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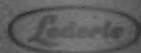


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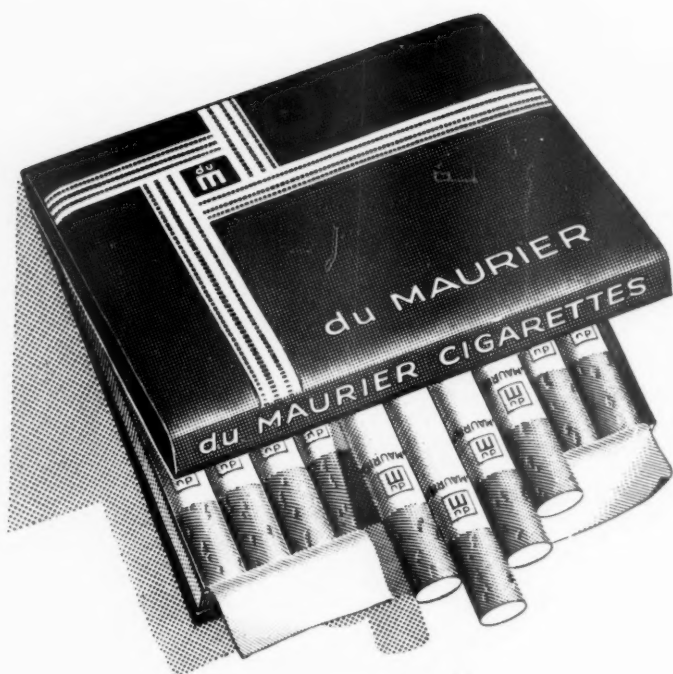
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BOOK REVIEWS

The Teaching and Learning of Psychotherapy.

By Rudolf Ekstein, Ph.D., and Robert S. Wallerstein, M.D. (Pp. xvi + 334. 42s.) London: Imago Publishing Co. Ltd. 1958.

This is a sincere attempt to describe the phenomenology associated with the teaching and learning of psychotherapy. As Dr. Lewin states in his foreword, the pupil can be compared with the intending surgeon who begins his career as an assistant at operations. There is, however, one important difference. The surgical assistant and his teacher usually keep the emotional reactions evoked by their work to themselves, but their opposite numbers in psychotherapy are subjected here to a close and lengthy scrutiny.

The work arises from a firm belief in the validity and usefulness of a psychoanalytically orientated kind of psychotherapy; and a review which did not take account of this fact would be less than fair. A general psychiatrist may feel resistance to the erection of a therapeutic problem out of what to him is a simple social encounter. Indeed many go to elaborate lengths to ensure that colleagues are not treated as patients, and there is little doubt that life is rather simpler if this is done.

This is a view not shared by the writers of the book but they have not hesitated to consider it and to put forward their reasons why it should not prevail. The findings set forth may not be found helpful in an undergraduate medical school, but in an institute devoted largely to psychoanalytic techniques they will be found both interesting and practical.

Centaur. Essays on the History of Medical Ideas.

By Felix Martí-Ibáñez, M.D. (Pp. xvii + 714. \$6.00). New York: MD Publications, Inc. 1958.

In his introduction to this book the author refers to it as fragments of his thought—a selection from a “mass of words scattered through time and space in domestic and foreign magazines”. To the English reader of liberal culture it will appear that this is exactly what it is. Dr. Martí-Ibáñez, having declared in the first chapter that the physician should learn that it is better to know a few classic authors and universal themes thoroughly than all authors and themes superficially, goes on to admit that he himself is inclined “to worship encyclopædic knowledge, but only a cultural encyclopædism, the kind that affords one a panoramic view of human learning

through time and space”. This he has undoubtedly done in a large volume of 700 pages, containing innumerable references to medicine, pathology, art, literature, and philosophy. The work as a whole strikes one as a heterogeneous gallimaufry of impressions.

As a collection of references, it may possibly be of some use to a reader who is making some preliminary notes of subjects which he hopes to study at a later date. As a cultural work, it hardly deserves approbation. The literary style is wearisome, and resembles that of the journalist who seeks to hide his lack of fundamentals under a mass of florid verbiage, and can only distress those readers who are accustomed to the clarity and simplicity of the real masters of English prose.

Bleeding Esophageal Varices—Portal Hypertension.

By Hirsch Robert Liebowitz, B.S., M.D. (Pp. xxxiii + 986; illustrated. £9 3s. 6d.) Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

In the foreword to this volume Dr. Whipple states that bleeding from ruptured oesophageal varices carries a greater mortality than bleeding from any other lesion of the digestive tract. From a review of a modest group of fifty deaths from this cause in the Bellevue Hospital, New York, the author has expanded this material to a volume of nearly 1,000 pages which is encyclopædic in its scope. Reference is made to a very large number of published papers on the subject. Some of the older views which are no longer tenable are given undue space, but among all this material the reader will find answers to a great many of the problems of this complex syndrome. After chapters on the anatomy, physiology and pathology of the portal system, and of the conditions of the liver which cause portal obstruction, the clinical aspects are discussed, and the book is quite up to date in its description of portal-systemic encephalopathy and the emergency management of bleeding varices.

The chapters dealing with surgical treatment have been written in collaboration with Dr. L. M. Rousselot and this surgeon's long experience is reflected in the sound judgment given in the management of these patients.

The price of the book will put it out of the range of most doctors in this country, but as a source of reference it will be invaluable to the specialist.

Treatment of Cancer and Allied Diseases. Edited by George T. Pack, M.D., F.A.C.S., and Irving M. Ariel, M.D., F.A.C.S. 2nd ed. To be published in 9 volumes. Vol. I: Principles of treatment. (Pp. xxi+646; illustrated. £8.) London: Pitman Medical Publishing Co., Ltd. 1958.

The second edition of this well-known work on cancer comprises nine volumes, as compared with three volumes in the first edition. The objective is to bring together in one work the great mass of information concerning the techniques of all varieties of cancer treatment used at present. The subject matter of the volumes is presented on a regional basis and the treatments described are those best suited for a given histological type of cancer.

It is right that the prevention of cancer should form the subject matter for chapter 1. This is written by W. C. Hueper who stresses the importance of the preventive approach for controlling cancer. There follow chapters dealing with the organization of a tumour clinic in a general hospital, of cancer detection facilities and of home care of the cancer patient. The section concerning surgery opens with the general principles of pre-operative and post-operative care. These matters are applicable to all major surgical cases, but it is rightly pointed out that certain cancers have deleterious effects upon the patient's metabolism and hence on his ability to undergo major surgical operations. Other chapters in this section deal with the problems of operative risk, including the pre-operative preparation of the poor-risk patient, with electro-surgical treatment, and with special considerations of vascular surgery pertaining to the treatment of malignant neoplasms including bilateral removal of the internal jugular veins: the authors draw attention to the safety of this procedure when done in two stages. A temporary tracheostomy is advisable when bilateral ligation is anticipated in the presence of laryngeal oedema. Nearly 40% of the subject matter is concerned with the various aspects of radiotherapy. R. Phillips has written on supervoltage X-ray therapy, and the chapter on the clinical application of the radium element pack (known in this country as radium beam therapy or telerradium therapy) was entrusted to Constance Wood.

The use of radioactive cobalt and other subjects are described in subsequent chapters. Hormone therapy, chemotherapy and general care of the cancer patient are dealt with in five chapters which are of special interest. The volume ends with two chapters on problems connected with reporting end-results of cancer treatment.

Bibliographies are grouped at the end of the book. In some chapters these are very short, and the whole bibliography has rather an aged look.

The emphasis in these nine volumes is on treatment and Pack and Ariel have made a good start on their hard task. This volume is well produced and the whole work is a welcome addition to cancer literature.

Atlas Intracardialer Druckkurven. By Prof. Dr. Otto Bayer and Dr. Hans Helmut Wolter. English translation by G. R. Graham, M.D. Spanish translation by Dr. E. Low-Maus. (Pp. 185; illustrated. DM. 68.) Stuttgart: Georg Thieme Verlag. 1959.

This atlas will be welcomed by many as a helpful guide to the interpretation of pressure records obtained at cardiac catheterization. The records illustrated in this book are almost all made during right heart catheterization, although one or two examples of left heart pressure records, either by retrograde aortic catheterization or direct left atrial puncture, are included. The normal physiological pressure relationships between the various chambers and vessels are described and illustrated. The diseases considered are pulmonary stenosis, ventricular and atrial septal defect, patent ductus arteriosus, coarctation of the aorta, tricuspid and mitral valve disease with special emphasis on the differentiation between stenosis and incompetence in the latter, and constrictive pericarditis. Wedge pressure records in mitral valve disease are fully discussed and compared with pressures recorded directly from the left atrium.

The illustrations are of excellent quality and the text in German, English, and Spanish clear and concise. Special emphasis is placed on the recognition of common artifacts that may cause confusion in interpretation.

A Concise Textbook for Midwives. By Douglas G. Wilson Clyne, B.M., B.Ch., M.A.(Oxon.), L.R.C.P., F.R.C.S.(Edin.), F.R.C.O.G., Barrister-at-Law. (Pp. 317; illustrated. 32s. 6d.) London: Faber and Faber, Ltd. 1959.

This new textbook for midwives is, as the title implies, deliberately concise. It is based mainly on questions set during seventeen years by the Central Midwives Board and the Central Midwives Board for Scotland. It thus covers most of the topics on which a pupil midwife is likely to be questioned in her examination as well as subjects which are outside the scope of midwives' examinations.

Because the book is written in a concise form

under many headings and sub-headings the text is as a whole not very readable. Nevertheless it should prove valuable as a book for revision and quick reference.

Bigger's Handbook of Bacteriology. Revised by F. S. Stewart, M.D.(Dublin), F.R.C.P.I. 7th ed. (Pp. x+611; illustrated. 37s. 6d.) London: Baillière, Tindall & Cox. 1959.

The main merit of Bigger's Handbook has always been that it gives the medical student the essential facts he needs to know and at the same time sets out the broad principles of the subject in an interesting way. The present edition keeps up the high standard of its predecessors. There are two main changes in emphasis: much more space is devoted to the subject of chemotherapy which has made great advances in the ten years since the previous edition and the viruses also receive nearly three times the amount of space formerly devoted to them.

There are two notable omissions in this as in previous editions. Although from time to time the work of various bacteriologists is mentioned and they are mentioned by name, no references are given nor is there a bibliography. There is no reason why, even in a book intended primarily for medical students, a certain number of key references should not be given and there is every reason for referring the student to other sources so that he may from time to time at least read something in the original papers.

It is also unfortunate that more attention is not devoted to epidemiology. This is clearly one of the most important aspects of bacteriology and one that is often neglected in the medical curriculum. One of the outstanding advances in recent years has been the growth of the Public Health Laboratory Service in this country and the subject of diagnostic bacteriology cannot be adequately considered without reference to the methods of this Service and the great help which it can give in the investigation of epidemics.

It would have been difficult to have made drastic alterations in this edition without considerably altering the character of the work but these two changes might have been introduced when bringing the handbook up to date.

On the whole the new edition has maintained an admirable standard and Professor Stewart is to be congratulated on the way he has succeeded in carrying out this difficult task.

Early Diagnosis. Edited by Henry Miller, M.D., F.R.C.P. (Pp. viii+400. 25s.) Edinburgh and London: E. & S. Livingstone Ltd. 1959.

This is an excellent volume of contributions by numerous authors, each an expert in his own

subject, with the clinical approach to early diagnosis brilliantly summarized by Lord Cohen in the opening chapter.

The scope of subjects included is perhaps a little too broad and goes beyond the limits of the purpose set out in the preface as a book to help the general practitioner in the early recognition of important disease. Such subjects as psychosis, skin diseases and deafness hardly come within this definition and their inclusion tends to upset the balance of the book—for example chronic alcoholism occupies 18 pages whereas the far more important subject of the early diagnosis of poliomyelitis is limited to 8 pages.

There can be little criticism of the individual articles. One surprising statement is that pain is an early symptom of cancer of the lung. Several authors ascribe an almost academic importance to the history of a case. "If the evidence of the history and the physical examination appear to disagree the history is often the more reliable." Fortunately this statement is exactly contradicted by another contributor who states that "when the history appears to conflict with physical findings on examination the history is likely to be the less reliable". Differences of opinion among the experts are to be expected and respected for they stimulate thought among the readers, which is one of the main purposes of a book.

The articles are all well written and very readable and the book is excellent value.

Orthopaedic Surgery. By Sir Walter Mercer, M.B., Ch.B.(Edin.), M.Ch.Orth.(Liv.) (Hon.), F.R.C.S.(Edin.), F.A.C.S.(Hon.), F.R.C.S.(Eng.) (Hon.), F.C.S.So.Af. (Hon.), F.R.C.S.I.(Hon.), F.R.S.(Edin.). 5th ed. (Pp. xi+1075; illustrated. 90s.) London: Edward Arnold (Publishers) Ltd. 1959.

The call for a fifth edition of this admirable textbook is sure evidence of its popularity, not only among budding orthopaedic surgeons but also among medical students as orthopaedics assumes ever greater importance in their teaching.

The whole text has been thoroughly revised and, as far as possible in so rapidly changing a scene, brought up to date. In spite of competition from the South, Sir Walter can be sure that the popularity of this now classic textbook will be deservedly maintained.

The Recovery Room. A Symposium edited by John Adriani, M.D., and John B. Parmley, M.D. (Pp. xii+123; illustrated. 32s. 6d.) Oxford: Blackwell Scientific Publications. 1958.

The laudable purpose of this small treatise is to provide information on the planning and

administration of post-operative recovery rooms, for the benefit of those hospital authorities and medical and nursing staff who are as yet unconvinced of their advantages, or who may be concerned in their design.

The contributors include anaesthetists, surgeons, senior nursing staff and hospital administrators, and most of them favour a generous establishment of recovery beds—between 1½ and 2 beds or trolley stations per operating theatre. Further evidence of transatlantic thinking is shown by the eight pages devoted to costing and by the assumption that nurse anaesthetists are employed.

In spite of the many distinguished contributors, the total effect of this book is a little disappointing. It is couched in "question and answer" form, and not only is there much repetition but also considerable waste of space—barely two-thirds of the pages contain even 200 words of text.

Over a third of the contents are concerned with detailed instructions for nurses and with the listing of equipment, but the essential points—the definition, purposes and merits of recovery rooms and problems of responsibility and administration—are, nevertheless, briefly discussed.

Physiology of Spinal Anaesthesia. By Nicholas M. Greene, B.S., M.A., M.D. (Pp. xi+195; illustrated. 48s.) London: Baillière, Tindall & Cox, Ltd. 1958.

Contrary to the often expressed view that spinal anaesthesia is now only of historical interest, this technique is not only often employed in this country but enjoys widespread popularity in many reputable centres abroad.

It is therefore essential that all anaesthetists, as well as others interested in this controversial subject, should have a thorough understanding of the physiological principles involved and of how they may be affected by analgesic drugs introduced into the cerebrospinal fluid.

To review the present state of knowledge in this field has been Dr. Greene's purpose, and he has succeeded admirably.

Clinical indications, details of techniques and consideration of the neurological complications are outside his terms of reference, but he has nevertheless reviewed several hundred papers—half of them published in the last ten years—on the effects of spinal anaesthesia on the various systems of the body. Of these, perhaps the most important is the sympathetic nervous system, and a large part of this monograph is devoted to a discussion of the many alterations in circu-

latory haemodynamics which may follow sympathetic blockade; this may be produced either by spinal and extradural analgesia, or by the many ganglion-blocking drugs used for hypotensive anaesthesia or in clinical medicine.

Writing with the authority of one who has had considerable clinical and research experience with spinal anaesthesia, Dr. Greene has produced an admirably objective and surprisingly readable book, which can be recommended not only to anaesthetists, but also to anyone interested in the effects of sympathetic nervous blockade.

Pregnancy, Birth and Abortion. By Paul H. Gebhard, Wardell B. Pomeroy, Clyde E. Martin and Cornelia V. Christenson. (Pp. xiii+282. 30s.) London: William Heinemann (Medical Books) Ltd. 1959.

From the Institute for Sex Research founded by the late Dr. Alfred C. Kinsey at Indiana University there have been two major contributions—"Sexual Behaviour in the Human Male" and "Sexual Behaviour in the Human Female". The present volume is an elaborate compilation of data based on interviews with 7,000 women in which they described their sex behaviour and reproductive experiences. The extent of pre-marital pregnancy, pre-marital birth and pre-marital abortion (spontaneous and induced) among the single women and the married women during their pre-marital years is fully documented.

Induced abortion was a fairly common event among women with pre-marital pregnancies. In 91% of the illegal abortions the termination was by operation, with only 10% due to the taking of drugs. In 6.4% of all abortions the operation was therapeutic. An unexpected finding was the low incidence of subsequent physical and psychological complications; there was no evidence of increased sterility.

The sexual and reproductive histories of negro females and of women in prison (white and coloured) have been compared. The striking finding was the low incidence of induced abortion in single negro women and the high numbers of spontaneous abortions and births out of wedlock.

In this book information is presented in a realistic, rational and objective way about a subject which is of the greatest sociological importance. Both lay and medical workers in the field of social medicine will find it of inestimable value. It is a unique compendium of facts never previously available, on a problem which affects many people throughout the world.

Proceedings of the International Symposium on Enzyme Chemistry, Tokyo and Kyoto 1957.

Organized by Science Council of Japan under the auspices of International Union of Biochemistry. (Pp. 541; illustrated. £6.) London, etc.: Pergamon Press, Ltd. 1958.

A detailed review of such a series of papers is hardly possible. In addition to one hundred and nineteen papers classified under the headings, enzyme group transfer, enzyme systems of hydrogen, oxygen and electron transfer, the formation of proteins and enzymes, and enzymes and industry, there are four special lectures on cytochromes, the Koji—a Japanese source of enzymes, the phosphate cycle and the Pasteur effect, and enzymology and mechanochemistry of tissues and cells. The very titles of the papers reveal how deeply enzyme chemistry is now involved in cellular metabolism including within its ambit problems of drug metabolism and the metabolism of tumours, tissues and tissue cells and micro-organisms. Some of the papers, despite their apparent limitation of subject matter, raise questions of much wider importance in the functional anatomy of cellular chemistry. The significance of many of the observations may still be obscure but the problems raised are all intriguing. The contributions are international although there is a certain preponderance of Japanese and American work. The Japanese editorial staff are to be congratulated on their handling of the papers most of which are in English—a few are in French or German; misprints are rare, and the general presentation is of a high standard. This is a book for the departmental library and the specialist and will reward careful study.

Principles and Practice in the Management of Surgical Patients. By A. Venugopal Mudaliar, M.S., F.A.C.S., F.I.C.S. (Pp. xii+500; illustrated. Rupees 20; 30s.)

Madras: G. S. Press. 1959.

This book falls into the category of a house surgeons' and registrars' vade-mecum. Your reviewer approached it with particular interest and sympathy as the first example that he had seen of a surgical textbook coming from independent India. It is a remarkable work. In simple numbered sentences, clear instructions are given on most of the problems that house surgeons and registrars are likely to meet in the management of surgical patients. In this way a very large amount of information is compressed within a small space, but without conveying the atmosphere of being "potted". The book is divided into a short general section on such fundamental subjects as shock, hæmorrhage,

fluid administration and anaesthesia; a long section on the special problems of operations in individual regions; and a final short section on such subjects as surgery in the diabetic, and radioisotopes. In general, the advice given is sound and up to date, and the book compares very favourably with other works of its kind. On the negative side, the text could be pruned with profit and there are some weak patches, e.g. Hirschsprung's disease is treated by sympathectomy and head injuries on the basis of the theories of Trotter. Again, a long list of pre-operative investigations which may be carried out is given under the different headings without any indication of which are the important routine investigations, and which are those called for only under special circumstances. But the chief impression left on your reviewer was that the Indian mind might be peculiarly suited to the writing of textbooks, and that he would be interested to see further examples.

Autopsy Diagnosis and Technic. By Otto Saphir, M.D. 4th ed. (Pp. xxiv+549; illustrated. 63s.) New York: Paul B. Hoeber Inc. London, etc.: Cassell & Co. Ltd. 1958.

This book, though unassuming in appearance, contains a wealth of information. For it is not merely limited to the technical aspects of the routine autopsy which is, nevertheless, more than adequately described with many illustrations. There is, for example, a chapter on authorization for autopsy which, although based upon American law, can be very profitably read by pathologists and clinicians in other countries especially in respect of the approach to relatives for permission for the examination. The chapters on the autopsy diagnosis and technique on medico-legal cases contain valuable information including notes on changes resulting from atomic bomb explosions. There is also a short chapter on the examination of bodies which have been exposed to a treatment with radioactive isotopes whilst another useful contribution is that on tissue banking techniques although clearly these may vary in different places. The main arrangement is in systems with details of each dissection but in addition there is information on autopsies on stillborns and infants. There are descriptions of various pathological appearances, in many cases supported by a table giving differential diagnosis. The book is compact and suitably portable. It is not only valuable for the "beginner" but contains much information for those who are long past that stage, including the chapter entitled "do or don't" and suggestions for quick orientation. Finally, there is a comprehensive list of weights and measurements of organs with a preliminary word of caution.

Practical Obstetric Problems. By Ian Donald, M.B.E., M.D.(Lond.), F.R.C.O.G. 2nd ed. (Pp. xvi+712; illustrated. 55s.) London: Lloyd-Luke (Medical Books) Ltd. 1959.

The reviewer enjoyed reading the first edition of this book and has still more enjoyed reading this edition in which many changes and considerable enlargement are evident. For the preface the author indicates many of the variations which have occurred in obstetric thought and practice since the first edition and one is thereby tempted to turn up the appropriate sections and read the latest views. But it soon becomes clear that reading this book systematically is easy and pleasurable; the style is fluent—almost conversational, the teaching is emphatic and Professor Donald is not afraid to give his personal opinions as well as the accepted views. Nevertheless orthodoxy is paramount and when there are two opposing lines of thought, e.g. the treatment of septic abortion, both sides of the question are dealt with clearly and fairly.

It is impossible in a short review to consider in detail the subject matter. It will suffice to say that this book contains a wealth of material, so much so that its general standard is distinctly more advanced than is required by the average student reading for his final examinations. But it is admirably suited to the postgraduate or the particularly interested student and for all those reading for the higher qualifications or intending to make a special study of obstetrics.

The present edition is, as was the first, profusely and clearly illustrated and the list of references at the end of each chapter is sufficient for all ordinary purposes. A very good book.

Hernia. By Sir Heneage Ogilvie, K.B.E., M.A., M.Ch., M.D., F.R.C.S. (Pp. 135; illustrated. 28s.) London: Edward Arnold (Publishers) Ltd. 1959.

The treatment of hernias, particularly of inguinal hernias, continues to be a major incompletely solved problem of surgery. Sir Heneage Ogilvie has always regarded hernias as a worthy challenge to any surgeon, and surgeons will welcome this short clear expression of his mature views, phrased with characteristic felicity and based on great experience. He has confined his attention to the traditional hernias, and has not discussed hiatus hernia which is running true to type in the difficulties of its treatment. For inguinal hernias requiring more than removal of the sac, Sir Heneage advocates a combination of a Bassini-type procedure (though he condemns the classical Bassini operation), and a Handley reinforcing darn of the reconstructed posterior wall (though he does not mention Sampson Handley). He describes, and gives reasons why

he does not favour, the other operations generally employed. For femoral hernias, he advocates an extraperitoneal approach as "the standard method", and has clearly not been influenced by Sampson Handley's view that these operations reminded him of knocking down the back of the house to repair the front door. He regards the low operation for femoral hernia as "traditional rather than scientific". And this brings one to the weakness of the work. "Science is measurement" may be an incomplete definition, but some statistical support for the numerous dogmatic statements made throughout the book, many on controversial points, ought surely to have been furnished. As it is, we have to rely almost entirely on unsupported expressions of opinion. This major weakness apart, the book is delightful and profitable to read. Incidentally Halsted's name is incorrectly spelt on p. 13 and again (twice) on p. 84.

Wolff's Diseases of the Eye. Revised by Redmond J. H. Smith, D.O., M.S., F.R.C.S. 5th ed. (Pp. x+226; illustrated. 42s.) London: Cassell and Company Ltd. 1959.

This book describes in uncomplicated language and with a wealth of illustrations—many of them photographs—the common conditions which are met in the G.P.'s surgery and the out-patient department. It has been brought up to date and a comparison of the fourth with the present edition forcibly reminds the reader how many changes there are in the practice of ophthalmology and in the incidence as well as the management of disease. The chapter on glaucoma has been rewritten, reflecting the great advances in this subject. The retinopathies and uveal inflammations have received adequate attention and modern ideas are incorporated in their aetiology and recognition. The antibiotics receive full attention and the place of cortisone in ophthalmology is kept well in mind. A list of drugs with their dosage is drawn up towards the end of the book and this saves much needless repetition in the text. There is an excellent index. Many of Wolff's original pictures remain, especially those borrowed from his anatomy book and they remind us of an able and kindly teacher, always grateful to his mentor Percy Fleming, and unconsciously attracting to himself the devotion of young ophthalmologists. The author is to be congratulated on maintaining the format and spirit of the original textbook. There are changes where found necessary but the best has been retained and what has been added is up to the standard which Wolff set himself. Medical students and nurses should find this textbook just what they require and as an introduction to ophthalmology for a post-graduate, it can be firmly recommended.



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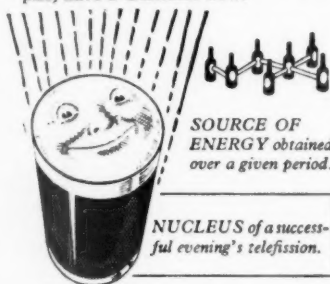
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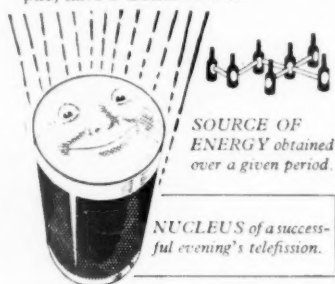
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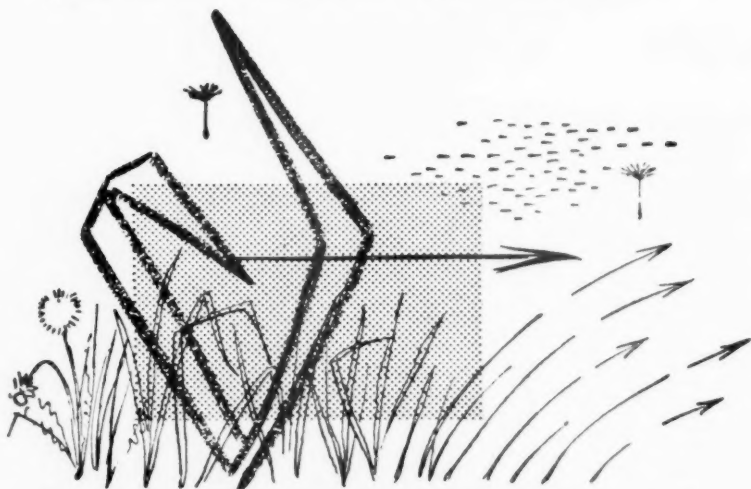
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 letter to
 "The Lancet" 11.10.58**

... Hytox has now been tried at one of our Hospitals with great success. The blankets emerged very white, soft and clean and the fibres have anti-bacterial properties and are sterile. Hytox is also inactivated by traces of ordinary washing soap in the blanket or in the crevices of the washing machine; so the first time a used blanket is washed the results may be disappointing. However, the second time the blankets are washed in a clean machine the results are very satisfactory.

Write for literature and testing sample to:

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